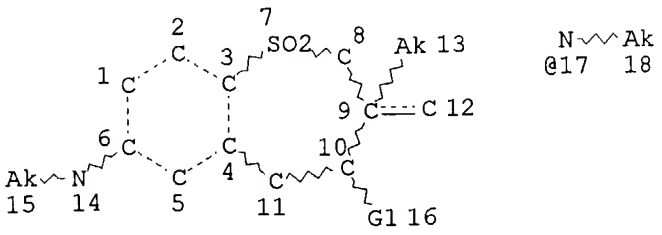
Krishnan
10/699967

(FILE 'REGISTRY' ENTERED AT 09:13:53 ON 26 AUG 2004)

L3 STR



VAR G1=H/OH/NH/17
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
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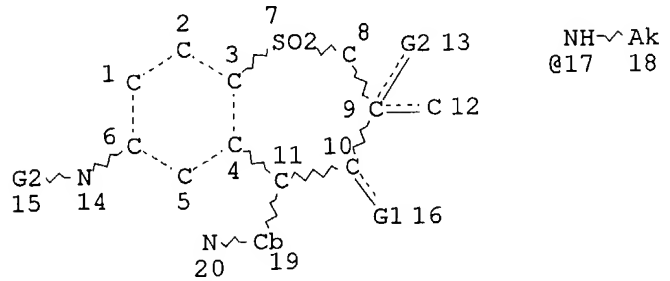
L8 STR



VAR G1=H/OH/NH/17
VAR G2=ME/ET/I-PR/N-PR/I-BU/N-BU/S-BU/T-BU
NODE ATTRIBUTES:
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GGCAT IS UNS AT 19
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L9 107 SEA FILE=REGISTRY SUB=L4 SSS FUL L8
L12 72 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND 1/NC

(FILE 'CAPLUS' ENTERED AT 09:29:57 ON 26 AUG 2004)
L13 13 S L12

E1 THROUGH E52 ASSIGNED

Searcher : Shears 571-272-2528

L13 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:492306 CAPLUS
DOCUMENT NUMBER: 141:17641
TITLE: Methods and compositions for the prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors
PATENT ASSIGNEE(S): Aventis Pharma SA, Fr.
SOURCE: Fr. Demande, 25 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2848452	A1	20040618	FR 2002-15722	20021212
WO 2004062652	A1	20040729	WO 2003-FR3654	20031210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004138145	A1	20040715	US 2003-734787	20031212
PRIORITY APPLN. INFO.:			FR 2002-15722 A	20021212
			US 2003-455354P P	20030317

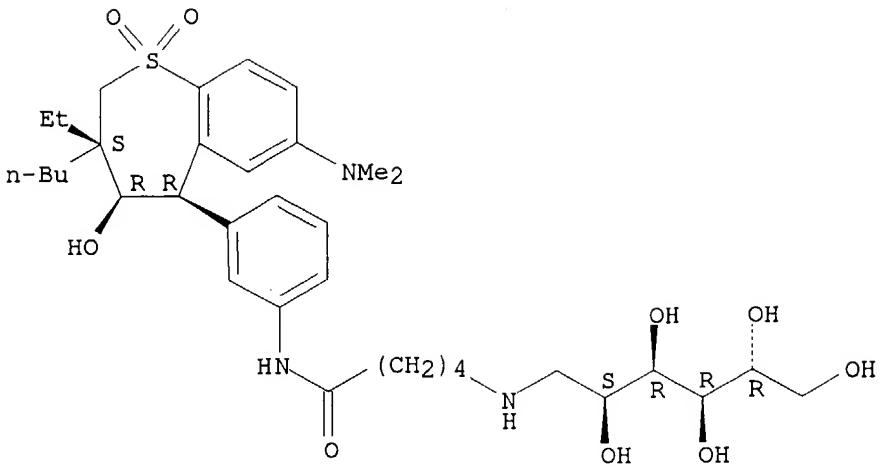
OTHER SOURCE(S): MARPAT 141:17641

AB The invention describe the application of the intestinal biliary acid reuptake inhibitors for the prevention and the treatment of Alzheimer's disease, alone or in conjunction with an HMG-CoA reductase inhibitor , a cholesterol uptake inhibitor, a cholesterol synthesis inhibitor or an inhibitor of APP secretases.

IT **252047-40-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)

RN 252047-40-8 CAPLUS
CN D-Glucitol, 1-[[5-[[3-[(3S,4R,5R)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]amino]-1-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:60147 CAPLUS
DOCUMENT NUMBER: 140:111291
TITLE: Preparation of substituted 5-aryl-benzothiepines as ileal bile acid transport and taurocholate uptake inhibitors
INVENTOR(S): Lee, Len F.; Banerjee, Shyamal C.; Huang, Horng Chih; Li, Jinglin J.; Miller, Raymond E.; Reitz, David B.; Tremont, Sanuel J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S. Pat. Appl. Publ., 235 pp., Cont.-in-part of U.S. Ser. No. 831,284.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004014803	A1	20040122	US 2002-68297	20020208
EP 1440972	A1	20040728	EP 2004-10088	19970311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AU 761249	B2	20030529	AU 2000-53394	20000816
US 2002013476	A1	20020131	US 2001-828968	20010409
US 6387924	B2	20020514		
US 2003171426	A1	20030911	US 2002-76091	20020215
US 6642268	B2	20031104		

PRIORITY APPLN. INFO.:

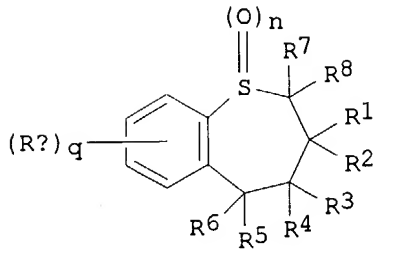
US 1994-305526	B2 19940913
US 1995-517051	B1 19950821
US 1996-13119P	P 19960311
US 1997-816065	A2 19970311
US 2001-828968	A3 20010409
US 2001-831284	A2 20010504

Searcher : Shears 571-272-2528

AU 1997-23266	A3	19970311
EP 1997-915976	A3	19970311
US 1997-40660P	P	19970311
US 1997-831284	B2	19970331
US 1997-68170P	P	19971219
US 1998-109551	A2	19980702
US 1999-275463	A1	19990324
US 1999-443403	A1	19991119
US 2000-676466	A3	20000929

OTHER SOURCE(S): MARPAT 140:111291

GI



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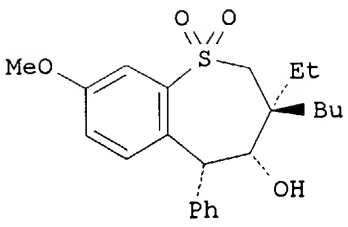
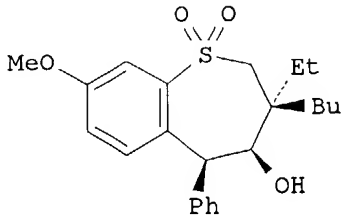


II



III

AB The title compds. (I) [wherein q = 1-4; n = 0-2; R1, R2 = H, (un)substituted (halo)alkyl, alkenyl, alkynyl, alkylaryl, arylalkyl, alkoxy(alkyl), dialkylamino, alkylthio, (polyalkyl)aryl, or cycloalkyl; or R1 and R2 taken together with the atoms to which they are attached = cycloalkyl; R3, R4 = H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocyclyl, OR9, NR9R10, SR9, S(O)R9, SO2R9, or SO3R9; R9, R10 = H, (cyclo)alkyl, alkenyl, alkynyl, aryl(alkyl), acyl, heterocyclyl, or ammoniumalkyl; or R3 and R4 together = :O, :NOR11, :S, :NNR11R12, :NR9, or :CR11R12; R11, R12 = H, (cyclo)alkyl, alkenyl, alkynyl, aryl(alkyl), heterocyclyl, carboxylalkyl, carboalkoxyalkyl, cyanoalkyl, OR9, NR9R10, SR9, S(O)R9, SO2R9, SO3R9, CO2R9, CN, halo, oxo, or CONR9R10; R5, R6 = H, alkyl, aryl, etc.; R7, R8 = H, alkyl; Rx = H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, polyalkyl, acyloxy, aryl(alkyl), halo(alkyl), (quaternary) heterocyclyl, (quaternary) heteroaryl, polyether, alkoxy, amino, alkylthio, NO2, carboxy, carbamido, etc.] were prepared for the prophylaxis and treatment of hyperlipidemic conditions, such as those associated with atherosclerosis or hypercholesterolemia.

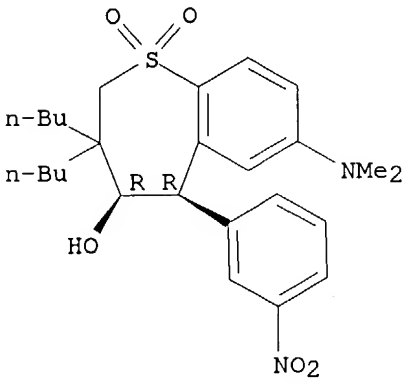
Thus, KOBu-t was added to a solution of 2-((2-benzyl-5-methoxyphenylsulfonyl)methyl)-2-ethylhexanal (preparation given) and dry THF

cooled to -1.6°C to give, after workup, II and III (96% combined yield). The isomers were separated upon recrystn. II inhibited IBAT-mediated uptake of [14C]-taurocholate in H14 cells with an IC50 of 0.1 μM and reduced serum cholesterol from 143 mg (7%) to 126 mg (2%) compared to control in cholesterol-fed hamsters in a 14-day test. In vitro taurocholate uptake assay data are included for nearly 600 compds. of the invention.

IT **197373-50-5P 197373-51-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

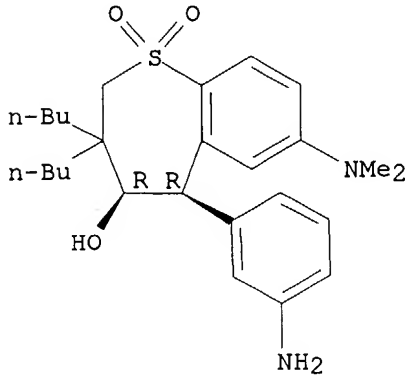
RN 197373-50-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 197373-51-6 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

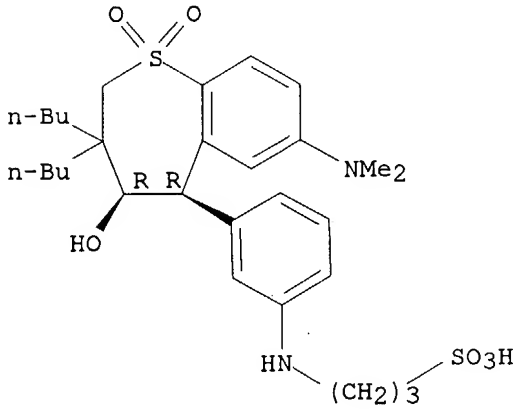
Relative stereochemistry.



IT **197373-37-8P 197374-04-2P 197374-59-7P 197375-96-5P 197376-55-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

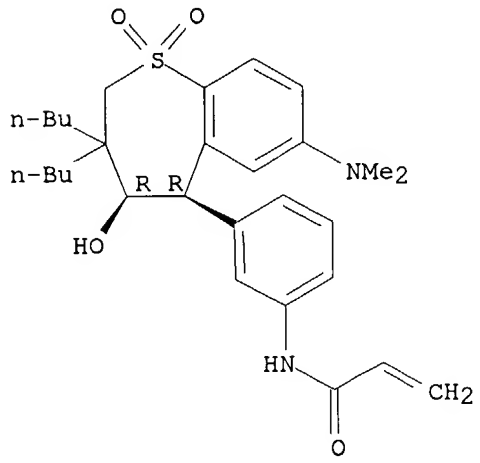
RN 197373-37-8 CAPLUS
CN 1-Propanesulfonic acid, 3-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



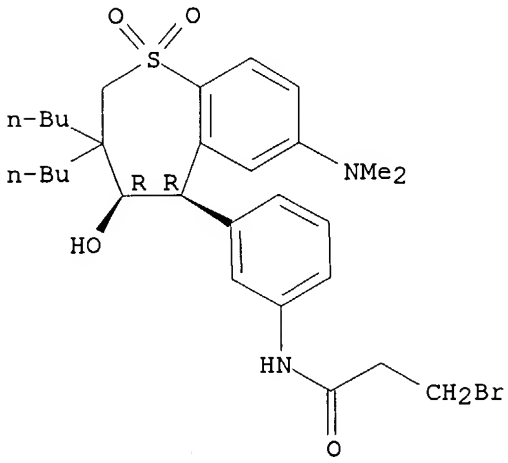
RN 197374-04-2 CAPLUS
CN 2-Propenamide, N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



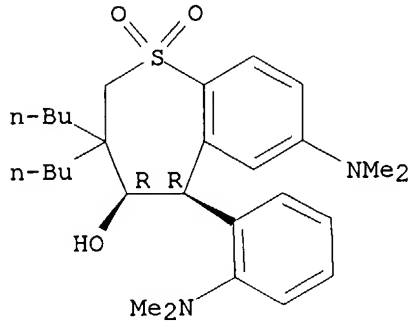
RN 197374-59-7 CAPLUS
CN Propanamide, 3-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



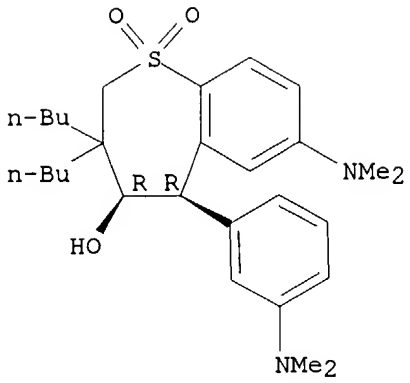
RN 197375-96-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[2-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 197376-55-9 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[3-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

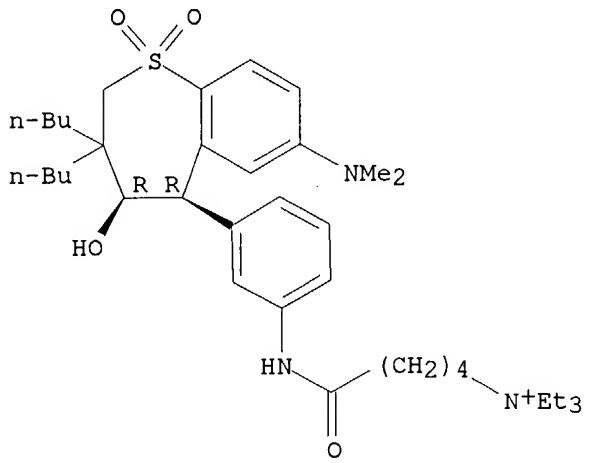


IT **197373-53-8P 280105-98-8P 647859-06-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

RN 197373-53-8 CAPLUS

CN 1-Pentanaminium, 5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-N,N,N-triethyl-5-oxo-, rel- (9CI) (CA INDEX NAME)

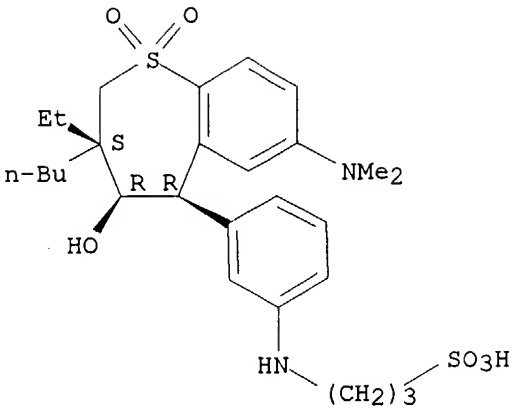
Relative stereochemistry.



RN 280105-98-8 CAPLUS

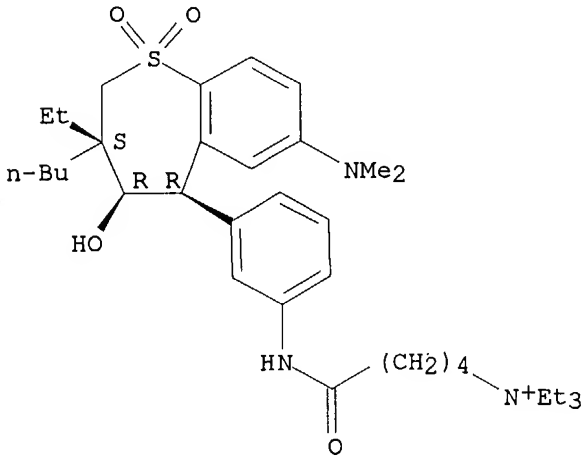
CN 1-Propanesulfonic acid, 3-[[3-[(3R,4S,5S)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 647859-06-1 CAPLUS
CN 1-Pentanaminium, 5-[[3-[(3R,4S,5S)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-N,N,N-triethyl-5-oxo-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L13 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:376848 CAPLUS
DOCUMENT NUMBER: 138:385315
TITLE: Mono- and di-fluorinated benzothiepines as inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions and methods for preparation
INVENTOR(S): Koeller, Kevin J.; Tremont, Samuel J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 589 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040127	A1	20030515	WO 2002-US35257	20021104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004067872	A1	20040408	US 2002-286987	20021104
US 6740663	B2	20040525		
EP 1448546	A1	20040825	EP 2002-778711	20021104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			US 2001-330892P	P 20011102
			WO 2002-US35257	W 20021104

OTHER SOURCE(S): MARPAT 138:385315
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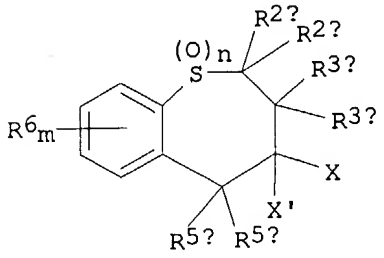


I

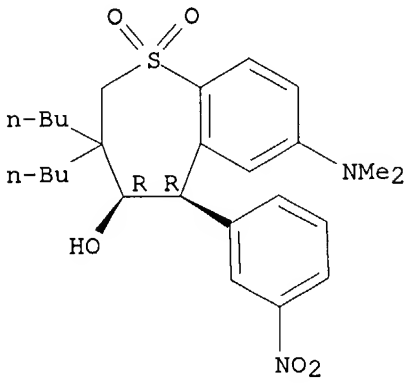
AB Mono-fluorinated and di-fluorinated benzothiepine apical Na co-dependent bile acid transport (ASBT) inhibitors (shown as I; variables defined below; no specific examples are included) are disclosed together with methods of making the same, methods of using the same to treat hyperlipidemic conditions as well as pharmaceutical compns. containing the same compds. For I: X = F, X' = H, F; n = 0-2; m = 0-4; R2A and R2B = H and hydrocarbyl; R3A, R3B, R5A, and R5B = H, alkyl, cycloalkyl, alkenyl, alkynyl, heterocyclyl, quaternary heterocyclyl, oxo, aryl-R5, -OR9, -NR9R10, -SR9, -S(O)R9, -SO2R9, and -SO3R9; R9 and R10 = H, hydrocarbyl, amino, and hydrocarbylamino. R5 = H, hydrocarbyl, heterocyclyl, quaternary heterocyclyl, -OR9, -SR9, -S(O)R9, -SO2R9, and -SO3R9; ≥1 R6 radicals = H, halogen, -CN, -NO2, hydrocarbyl, -R5, -OR13, -NR 13R14, -SR13, -S(O)R13, -S(O)2R13, -SO3R13, -S+R3R14A-, -NR13OR14, -NR13NR14R15, -OM, -SO2OM, -SO2NR13R14, -NR14C(O)R13, -C(O)OM, -S(O)NR13R14, -N+R13R14R15A-, -PR13R14, -P(O)R13R4, -P+R13R14R15A-, amino acid residue, peptide residue, polypeptide residue, and carbohydrate

residue; addnl. details are given in the claims. I (X = X' = F) are claimed to be preparable from the 4-oxo analog and diethylaminosulfur trifluoride; I (X = F; X' = H) are claimed preparable from the 4-hydroxy analog and diethylaminosulfur trifluoride. Hundreds of example prepns. of precursors to I are included, but none of I; most of the example prepns. have appeared in earlier patents (e.g. WO 98/40375). Biol. testing procedures are described but no test results are reported except for the statement that a polyethylene glycol-functionalized benzothiepine (4500 MW; a 4-hydroxy analog of I) inhibited ileal bile acid transport-mediated uptake of 14C-taurocholate in H14 cells.

IT **197373-50-5P 197373-51-6P 197373-52-7P**
289037-96-3P 289037-98-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

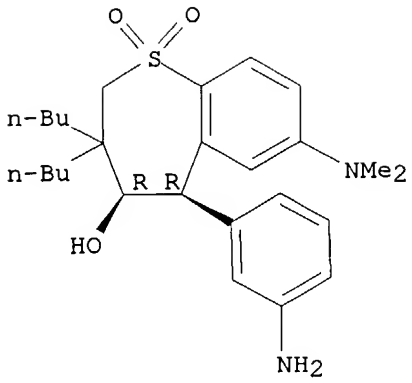
RN 197373-50-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



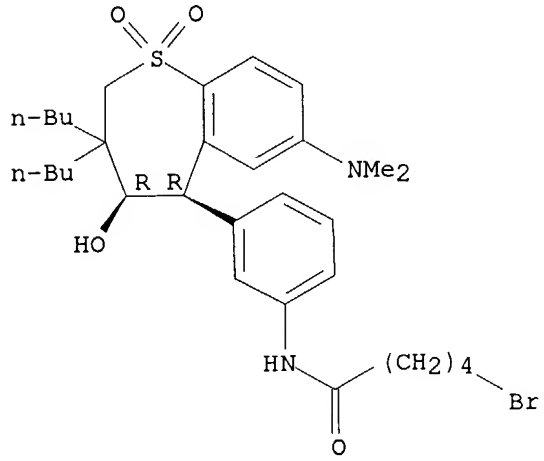
RN 197373-51-6 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



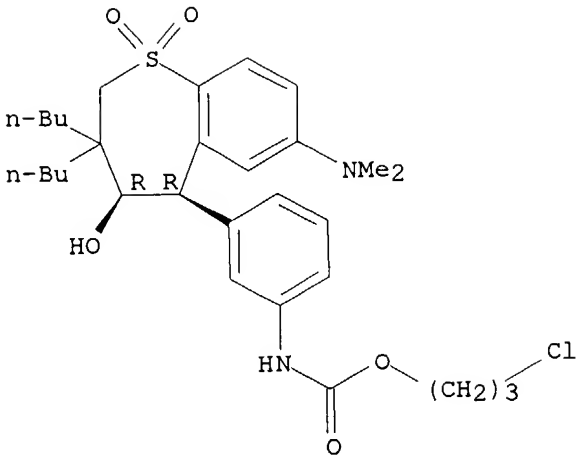
RN 197373-52-7 CAPLUS
CN Pentanamide, 5-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



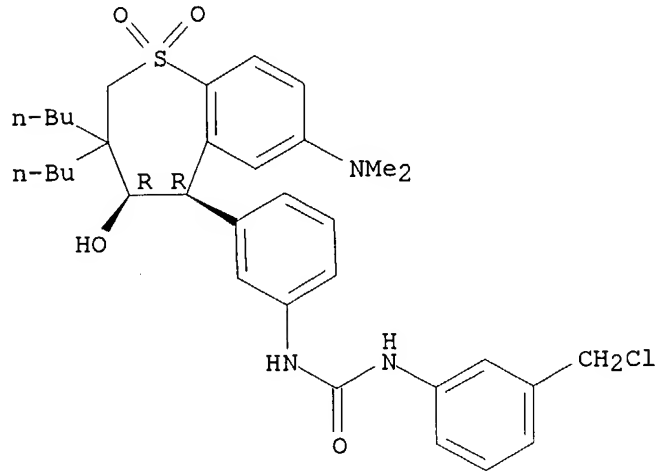
RN 289037-96-3 CAPLUS
CN Carbamic acid, [3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, 3-chloropropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

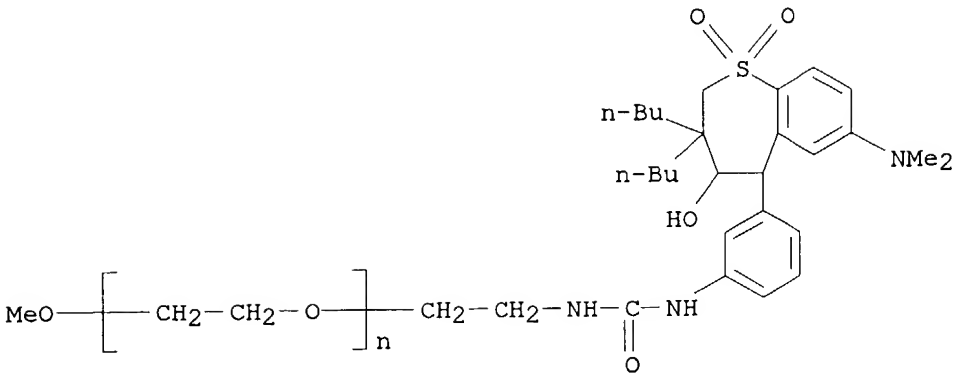


RN 289037-98-5 CAPLUS
CN Urea, N-[3-(chloromethyl)phenyl]-N'-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **280105-90-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)
RN 280105-90-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]carbonyl]amino]ethyl]-ω-methoxy-, rel- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

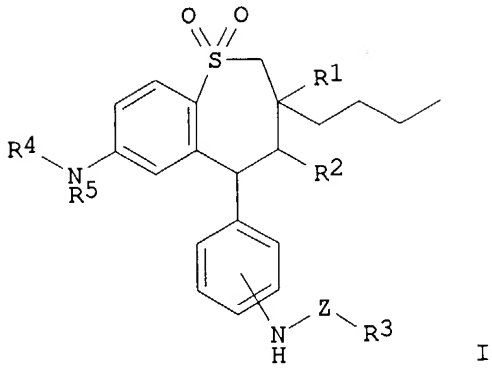
L13 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173440 CAPLUS
DOCUMENT NUMBER: 138:215326
TITLE: Combined preparations, containing 1,4-benzothiepine-1,1-dioxide derivatives and other active substances for the treatment of hyperlipidemia
INVENTOR(S): Glombik, Heiner; Frick, Wendelin; Schaefer, Hans-Ludwig; Kramer, Werner
PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018024	A1	20030306	WO 2002-EP8908	20020809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10140169	A1	20030306	DE 2001-10140169	20010822
DE 10142456	A1	20030320	DE 2001-10142456	20010831
EP 1425018	A1	20040609	EP 2002-796213	20020809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.:

DE 2001-10140169	A	20010822
DE 2001-10142456	A	20010831
WO 2002-EP8908	W	20020809

OTHER SOURCE(S): MARPAT 138:215326
GI



I

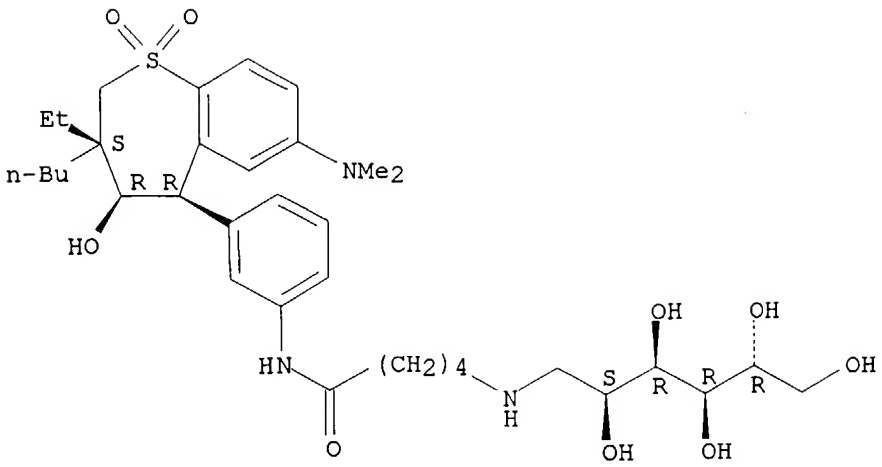
AB The invention relates to mixts. of substances, containing 1,4-benzothiepine-1,1-dioxide derivs. of formula (I), in which the functional groups have the indicated meanings, their physiol. acceptable salts and physiol. functional derivs. as well as other active substances for the treatment of metabolic disorders especially hyperlipidemia. The combinations can also include antidiabetics, antiarthrytics etc. A typical capsule contains 100 mg of the drugs and 400 mg triglyceride mixture from coco fatty acids; other formulations are emulsions, tablets, dragees, and solns. Hamster that were fed with cholesterol-rich feed received orally the drug combination once daily for 10 days. Feces was analyzed for bile acids, blood lipid levels were measured and cholesterol was determined from liver.

IT **252047-40-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

RN 252047-40-8 CAPLUS

CN D-Glucitol, 1-[[5-[[3-[(3S,4R,5R)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]amino]-1-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:487559 CAPLUS
DOCUMENT NUMBER: 137:63115
TITLE: Preparation of diphenylazetidinone derivatives as hypolipidemic agents
INVENTOR(S): Glombik, Heiner; Kramer, Werner; Flohr, Stefanie; Frick, Wendelin; Heuer, Hubert; Jaehne, Gerhard; Lindenschmidt, Andreas; Schaefer, Hans-Ludwig
PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050068	A1	20020627	WO 2001-EP14532	20011211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10064402	A1	20020627	DE 2000-10064402	20001221
DE 10154520	A1	20031002	DE 2001-10154520	20011107
AU 2002019173	A5	20020701	AU 2002-19173	20011211
EE 200300237	A	20030815	EE 2003-237	20011211
EP 1345932	A1	20030924	EP 2001-271371	20011211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001016482	A	20040203	BR 2001-16482		20011211
JP 2004516293	T2	20040603	JP 2002-551564		20011211
US 2002128252	A1	20020912	US 2001-21028		20011219
US 6498156	B2	20021224			
NO 2003002733	A	20030814	NO 2003-2733		20030616
PRIORITY APPLN. INFO.:			DE 2000-10064402	A	20001221
			DE 2001-10154520	A	20011107
			WO 2001-EP14532	W	20011211

OTHER SOURCE(S): MARPAT 137:63115
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

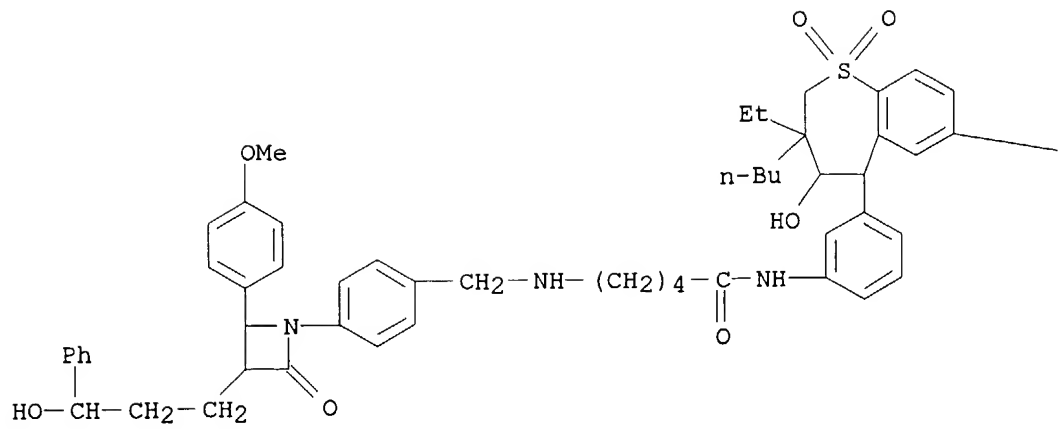
AB The compds. are suited for use e.g. as hypolipidemic drugs. The invention discloses preparation of diphenylazetidinone derivs. such as I [R1, R2, R3, R4, R5, R6 = C0-C30-alkylene-L {optionally containing O, CO, CH:CH, C.tplbond.C, N(alkyl), N(alkylphenyl), NH}, H, F, Cl, Br, I, CF3, NO2, CN, CO2H, CO2(alkyl), CONH2, CONH(alkyl), CON(alkyl)2, alkyl, alkenyl, alkynyl, O-alkyl, SO2NH2, SO2NH(alkyl) SO2N(alkyl)2, S-(alkyl), SO(alkyl), (un)substituted S(CH2)nPh, SO(CH2)nPh, SO2(alkyl), SO2(CH2)nPh, NH2, NH(alkyl), N(alkyl)2, NH(acyl), (un)substituted Ph, O(CH2)nPh; n = 0-6; L = II; R7, R9, R10 = Me, Et, Pr, butyl; R8 = H, OH, NH2, NH(alkyl)], and their physiol. acceptable salts, for their use as hypolipidemic agents. Thus, 1,2-diphenylazetidinone derivative III·trifluoroacetate (IV) was prepared via a multistep synthetic sequence starting from 7-[3-(3-butyl-7-dimethylamino-3-ethyl-4-hydroxy-1,1-dioxo-2,3,4,5-tetrahydro-1H-benzo[b]thiepin-5-yl)-phenylcarbamoyl]-heptanoic acid and 4-(4-aminomethylphenyl)-1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxyphenyl]-azetidin-2-one. Azetidinone IV was tested for its cholesterol lowering ability [ED50 = 0.01 mg/mouse].

IT **439113-82-3P 439113-89-0P 439113-91-4P**
439113-92-5P 439113-93-6P 439114-23-5P
439114-39-3P 439114-40-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diphenylazetidinone derivs. as hypolipidemics)

RN 439113-82-3 CAPLUS

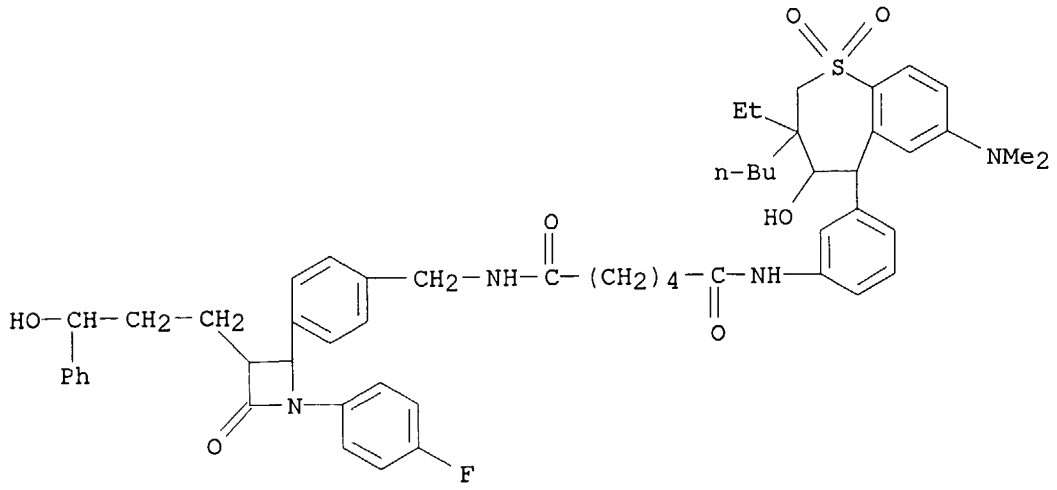
CN Pentanamide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-5-[[[4-[3-(3-hydroxy-3-phenylpropyl)-2-(4-methoxyphenyl)-4-oxo-1-azetidinyl]phenyl]methyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



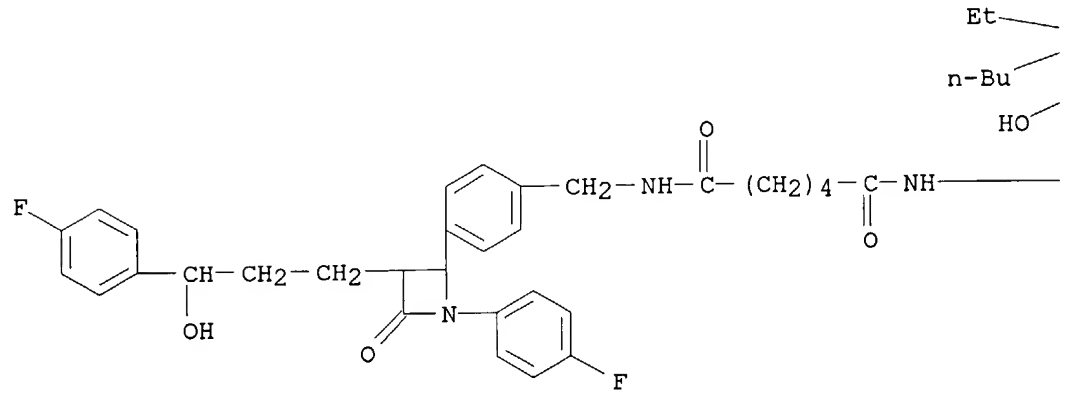
PAGE 1-B

RN 439113-89-0 CAPLUS
CN Hexanediamide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-N'-[[4-[1-(4-fluorophenyl)-3-(3-hydroxy-3-phenylpropyl)-4-oxo-2-azetidinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 439113-91-4 CAPLUS
CN Hexanediamide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-N'-[[4-[1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-oxo-2-azetidinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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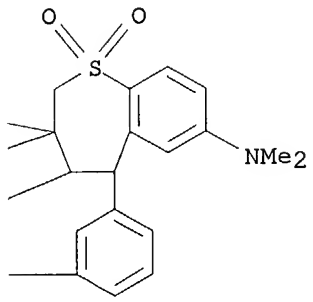
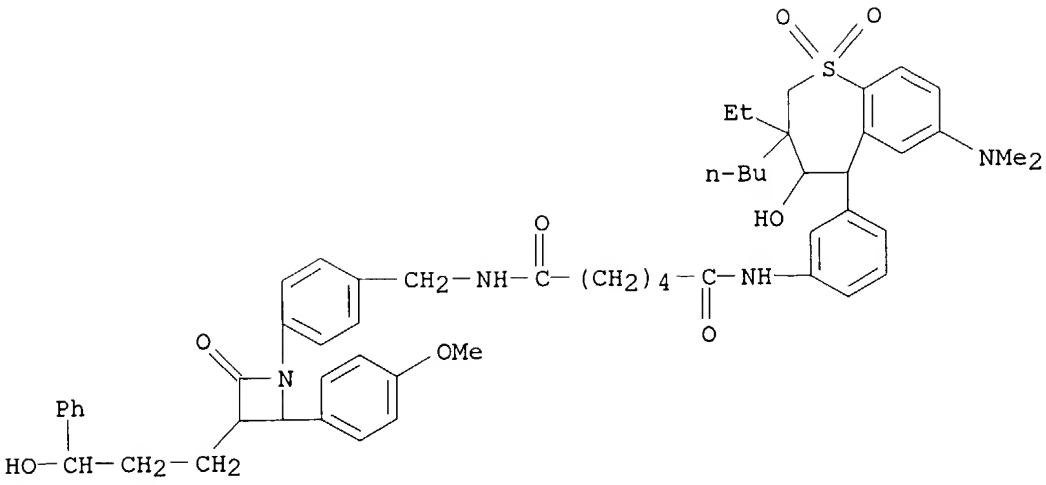
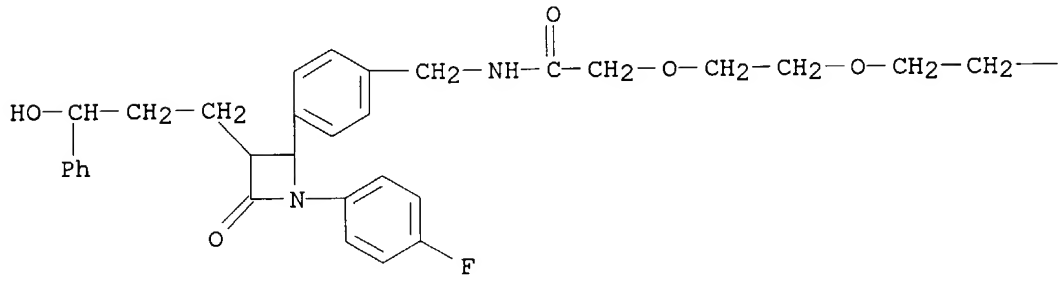
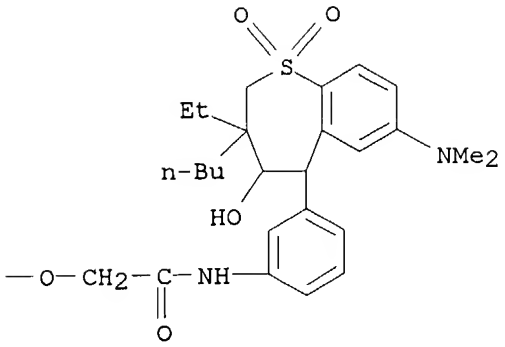


RN 439113-92-5 CAPLUS
CN Hexanediamide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-N'-[[4-[3-(3-hydroxy-3-phenylpropyl)-2-(4-methoxyphenyl)-4-oxo-1-azetidinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

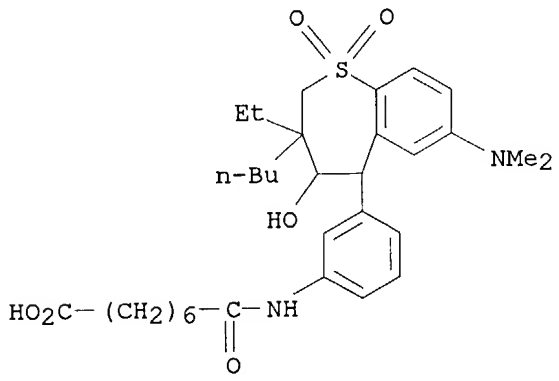


RN 439113-93-6 CAPLUS
CN 5,8,11-Trioxa-2-azatridecan-13-amide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-1-[4-[1-(4-fluorophenyl)-3-(3-hydroxy-3-phenylpropyl)-4-oxo-2-azetidinyl]phenyl]-3-oxo- (9CI) (CA INDEX NAME)



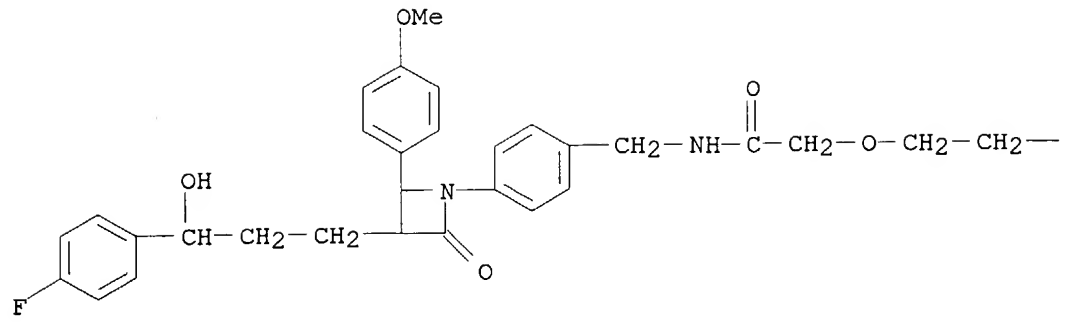


RN 439114-23-5 CAPLUS
CN Octanoic acid, 8-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-8-oxo- (9CI) (CA INDEX NAME)



RN 439114-39-3 CAPLUS
CN Acetamide, 2-[2-[2-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-2-oxoethoxy]ethoxy]-N-[[4-[3-[3-(4-fluorophenyl)-3-hydroxypropyl]-2-(4-methoxyphenyl)-4-oxo-1-azetidinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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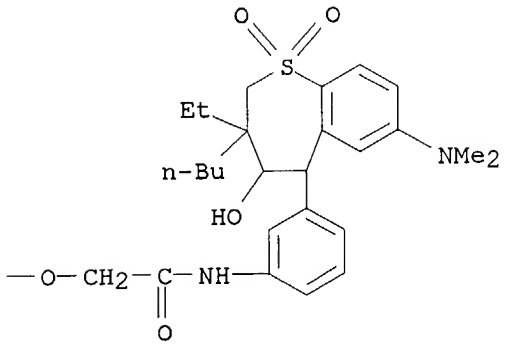
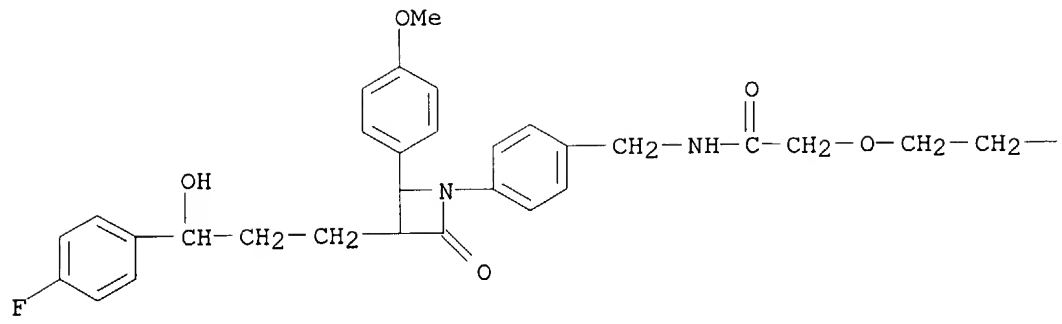


RN 439114-40-6 CAPLUS
CN 5,8,11-Trioxa-2-azatridecan-13-amide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-1-[4-[3-[3-(4-fluorophenyl)-3-hydroxypropyl]-2-(4-methoxyphenyl)-4-oxo-1-azetidinyl]phenyl]-3-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A



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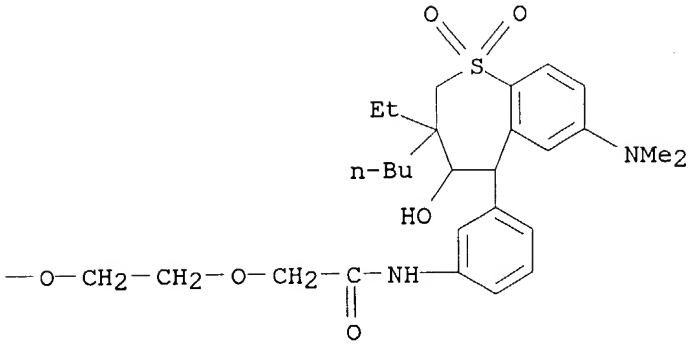
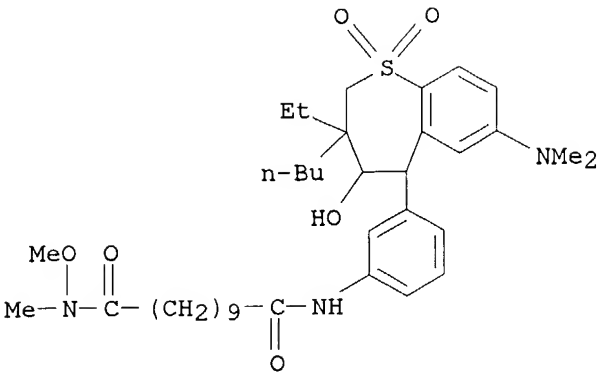
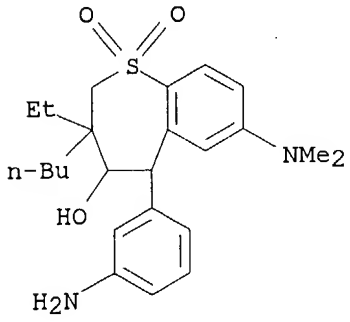


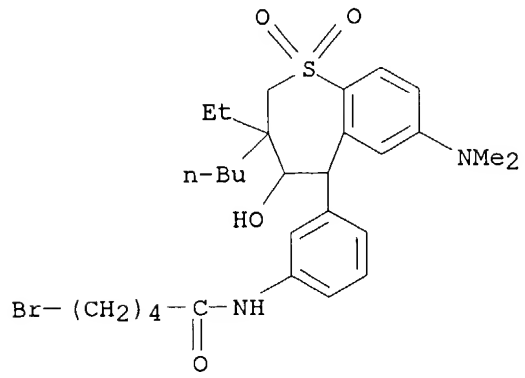
IT **439114-09-7 439114-42-8 439114-43-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diphenylazetidinone derivs. as hypolipidemics)
RN 439114-09-7 CAPLUS
CN Undecanediamide, N'-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-N-methoxy-N-methyl- (9CI) (CA INDEX NAME)



RN 439114-42-8 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-, 1,1-dioxide (9CI) (CA INDEX NAME)



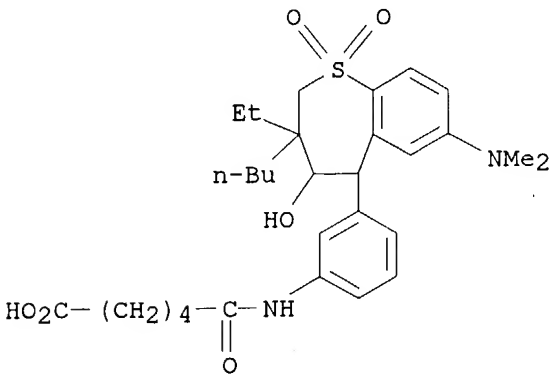
RN 439114-43-9 CAPLUS
CN Pentanamide, 5-bromo-N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]- (9CI) (CA INDEX NAME)



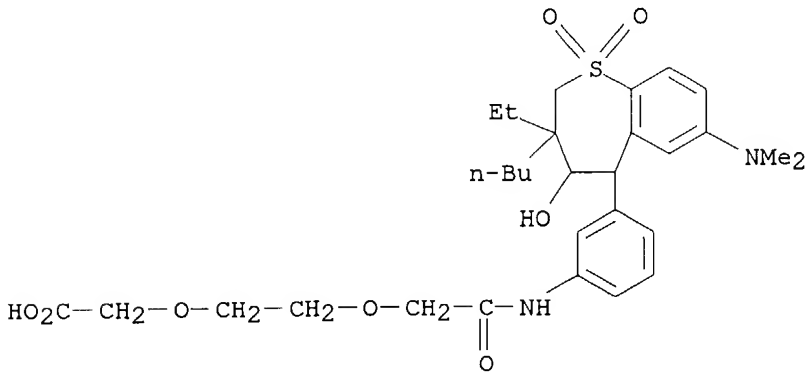
IT **439113-88-9P 439113-94-7P 439113-99-2P**

439114-04-2P 439114-14-4P 439114-18-8P
439114-24-6P 439114-27-9P 439114-32-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diphenylazetidinone derivs. as hypolipidemics)

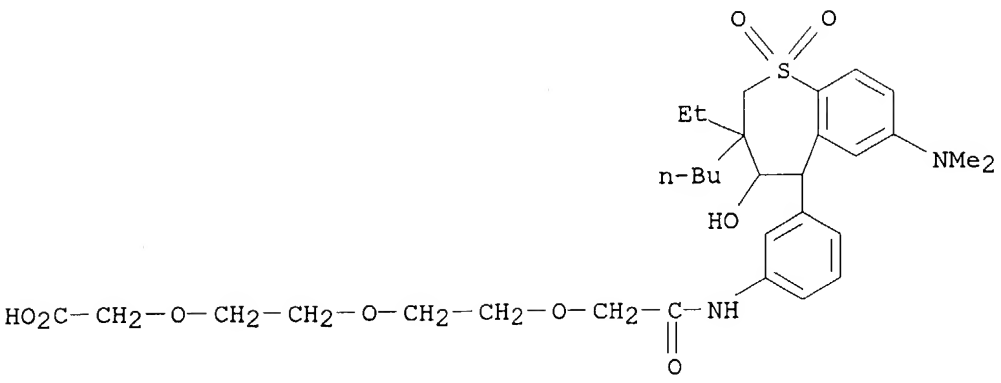
RN 439113-88-9 CAPLUS
CN Hexanoic acid, 6-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-6-oxo- (9CI) (CA INDEX NAME)



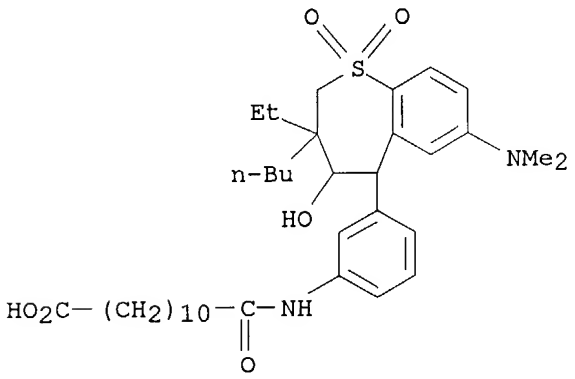
RN 439113-94-7 CAPLUS
CN Acetic acid, [2-[2-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-2-oxoethoxy]ethoxy]- (9CI) (CA INDEX NAME)



RN 439113-99-2 CAPLUS
CN Acetic acid, [2-[2-[2-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-2-oxoethoxy]ethoxy]ethoxy]- (9CI) (CA INDEX NAME)

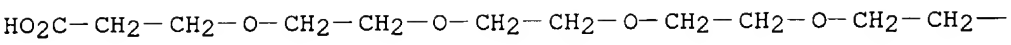


RN 439114-04-2 CAPLUS
CN Dodecanoic acid, 12-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-12-oxo- (9CI) (CA INDEX NAME)

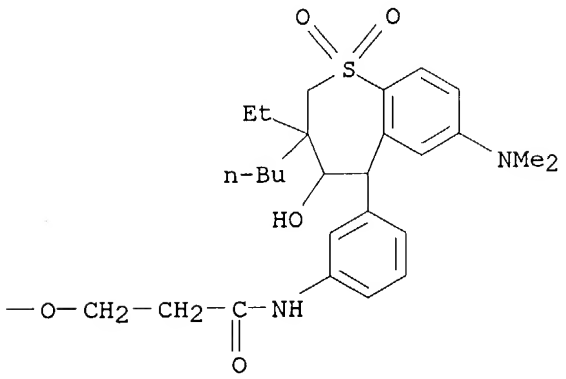


RN 439114-14-4 CAPLUS
CN 4,7,10,13,16-Pentaoxanonadecanoic acid, 19-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-19-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

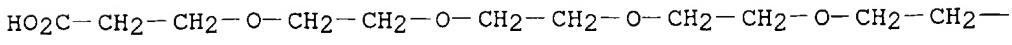


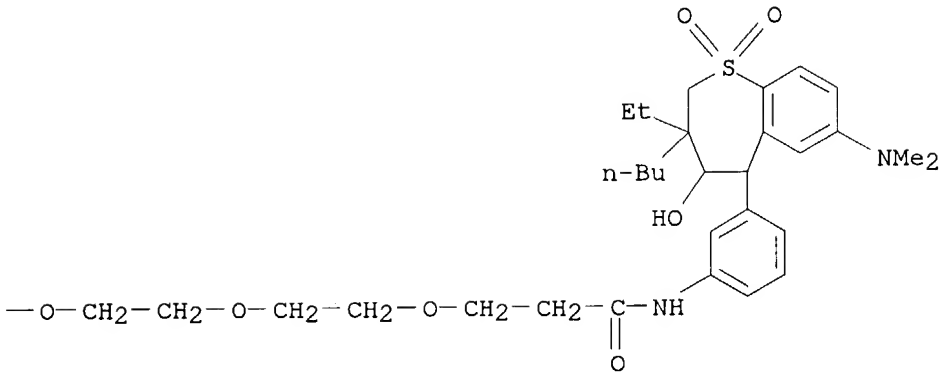
PAGE 1-B



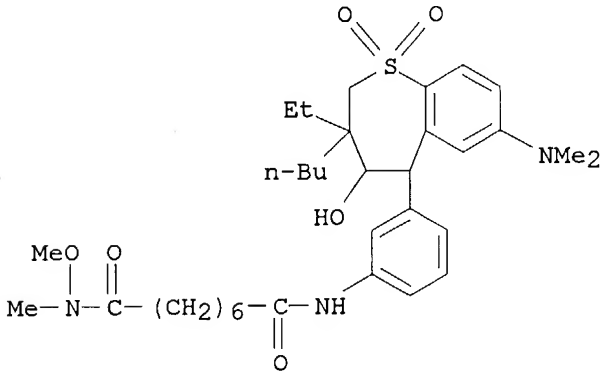
RN 439114-18-8 CAPLUS
CN 4,7,10,13,16,19,22-Heptaoxapentacosanoic acid, 25-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-25-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

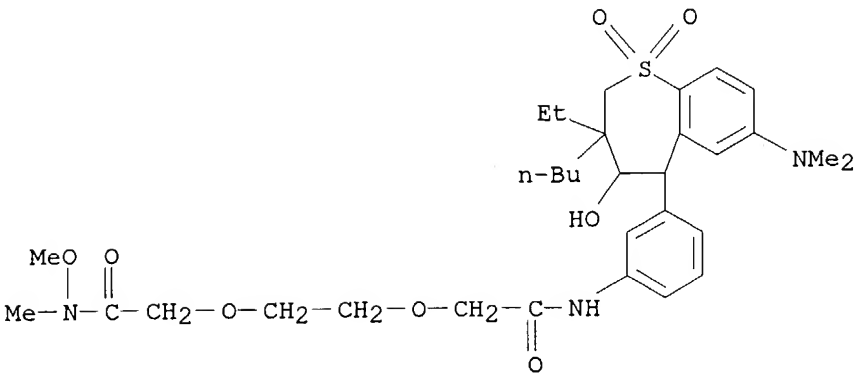




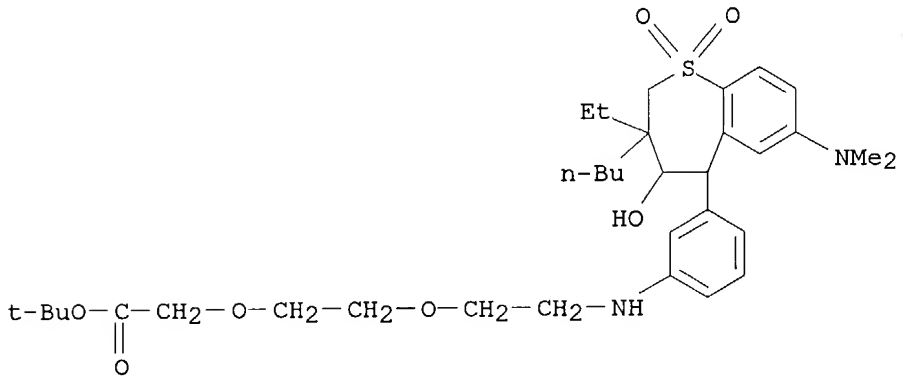
RN 439114-24-6 CAPLUS
CN Octanediamide, N'-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-N-methoxy-N-methyl- (9CI) (CA INDEX NAME)



RN 439114-27-9 CAPLUS
CN 2,6,9-Trioxa-3-azaundecan-11-amide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



RN 439114-32-6 CAPLUS
CN Acetic acid, [2-[2-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]ethoxy]ethoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2001:693092 CAPLUS
DOCUMENT NUMBER:	135:257253
TITLE:	Preparation of tetrahydrobenzothiepines and naphthalenes useful in combination therapy with HMG Co-A reductase inhibitors for the prophylaxis and treatment of hyperlipidemic conditions and disorders.
INVENTOR(S):	Keller, Bradley T.; Tremont, Samuel J.; Glenn, Kevin C.; Manning, Robert E.
PATENT ASSIGNEE(S):	Pharmacia Corporation, USA
SOURCE:	PCT Int. Appl., 182 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068096	A2	20010920	WO 2001-US7505	20010308
WO 2001068096	A3	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002061888	A1	20020523	US 2001-802313	20010308
US 2003232834	A1	20031218	US 2002-204672	20021126
US 2004082647	A1	20040429	US 2003-419266	20030421
US 2004110761	A1	20040610	US 2003-611942	20030703
PRIORITY APPLN. INFO.:			US 2000-188361P	P 20000310
			US 2000-188378P	P 20000310
			US 2001-802279	A3 20010308
			US 2001-802313	B1 20010308
			WO 2001-US7505	W 20010308

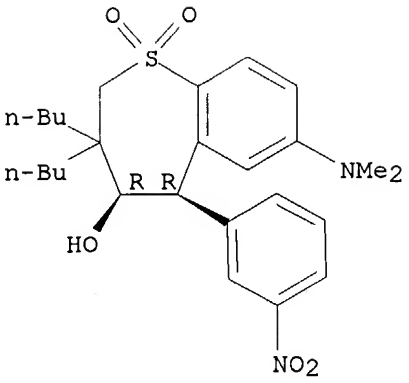
AB A method for the treatment and/or prophylaxis of a hyperlipidemic condition or disorder comprises the administration of ≥1 HMG Co-A reductase inhibitors and one or more specific apical Na codependent bile acid transporter (ASBT) inhibitors is claimed. Thus, (4R,5R)-1-[[4-[4-[3-butyl-3-ethyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxo-1-benzothiepin-5-yl]phenoxy]methyl]phenyl]methyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride (3,3-di-Bu analog preparation given) 0.375 mg/kg/day and lovastatin 0.45 mg/kg/day orally in dogs reduced serum triglycerides by 37% at 4 wk.

IT **197373-50-5P 197373-51-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tetrahydrobenzothiepines and naphthalenes useful in combination therapy with HMG Co-A reductase inhibitors for the prophylaxis and treatment of hyperlipidemic conditions and disorders)

RN 197373-50-5 CAPLUS

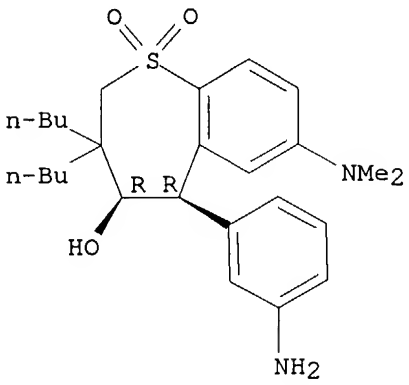
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 197373-51-6 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



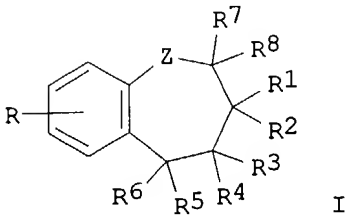
L13 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:560070 CAPLUS
DOCUMENT NUMBER: 135:137410
TITLE: Preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors.
INVENTOR(S): Keller, Bradley T.; Glenn, Kevin C.; Manning, Robert E.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 356 pp., Cont.-in-part of U.S. Ser. No. 831,284, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6268392	B1	20010731	US 1998-37308	19980309
EP 1440972	A1	20040728	EP 2004-10088	19970311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AU 761249	B2	20030529	AU 2000-53394	20000816
US 6420417	B1	20020716	US 2000-676466	20000929
US 2003171426	A1	20030911	US 2002-76091	20020215
US 6642268	B2	20031104		
US 2004157915	A1	20040812	US 2003-620460	20030717
PRIORITY APPLN. INFO.:			US 1994-305526	A2 19940912
			US 1995-517051	A1 19950821
			US 1996-13119P	P 19960311
			US 1997-40660P	P 19970311
			US 1997-816065	A2 19970311
			US 1997-831284	B2 19970331
			AU 1997-23266	A3 19970311
			EP 1997-915976	A3 19970311
			US 1998-37308	A3 19980309
			US 2000-676466	A3 20000929
			US 2002-76091	A1 20020215

OTHER SOURCE(S): MARPAT 135:137410

GI



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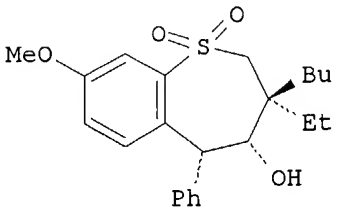


II

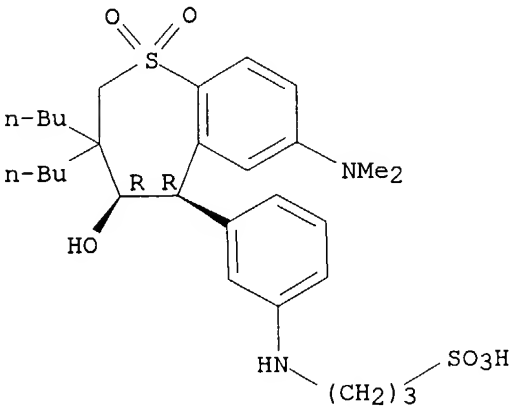
AB Title compds. [I; R = H or 1-4 of alkyl, alkenyl, alkynyl, acyloxy, aryl, aralkyl, halo, etc.; R1, R2 = H, (substituted) alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, alkoxy, dialkylamino, etc.; R1R2C = cycloalkylidene; R3, R4 = H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocyclyl, heteroaryl, etc.; R3R4 = O, S, NOR11, etc.; R11 = H, alkyl, alkenyl, alkynyl, aryl, aralkyl, etc.; R5, R6 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, etc.; R7, R8 = H, alkyl; Z = SO0-2], were prepared A composition comprising an ileal bile acid transport inhibitor and an HMG Co-A reductase inhibitor is claimed. Thus, title compound (II) (preparation via 2-mercapto-4-methoxybenzophenone given) at 0.2% as an ileal perfusion in guinea pigs reduced HDL cholesterol from 89 mg% to 76 mg%.

IT **197373-37-8P 197374-04-2P 197374-59-7P**
197375-96-5P 197376-55-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

Searcher : Shears 571-272-2528

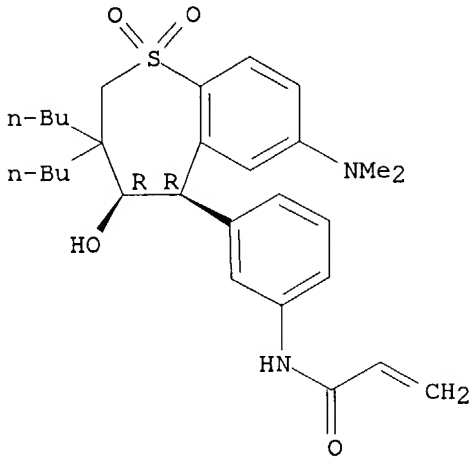
RN 197373-37-8 CAPLUS
CN 1-Propanesulfonic acid, 3-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



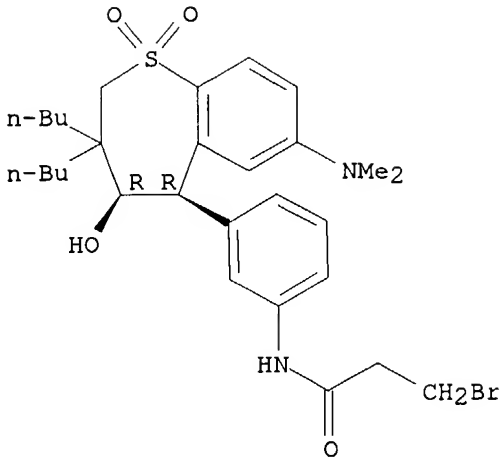
RN 197374-04-2 CAPLUS
CN 2-Propenamide, N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



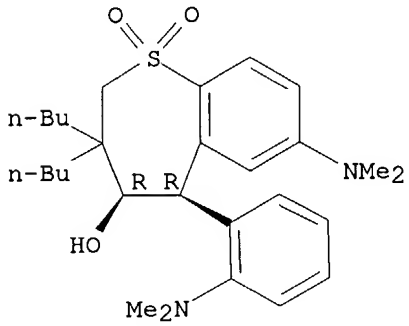
RN 197374-59-7 CAPLUS
CN Propanamide, 3-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



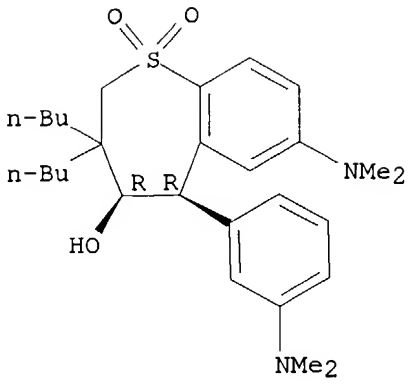
RN 197375-96-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[2-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 197376-55-9 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[3-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

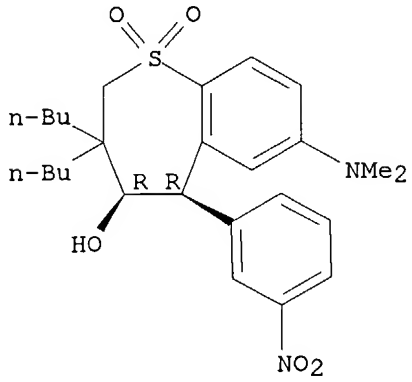
Relative stereochemistry.



IT **197373-50-5P 197373-51-6P 213312-74-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

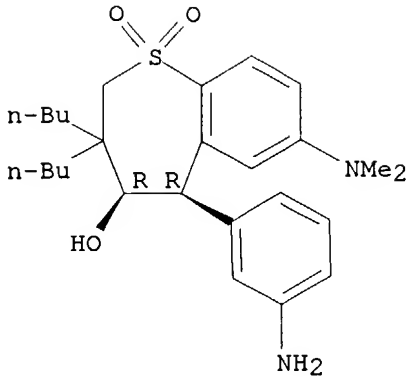
RN 197373-50-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



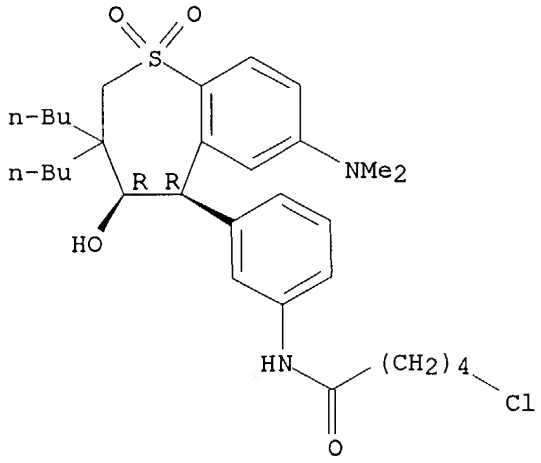
RN 197373-51-6 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 213312-74-4 CAPLUS
CN Pentanamide, 5-chloro-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:590035 CAPLUS
DOCUMENT NUMBER: 133:193089
TITLE: Preparation of substituted 5-aryl-benzothiepines as ileal bile acid transport and taurocholate uptake inhibitors
INVENTOR(S): Lee, Len F.; Banerjee, Shyamal C.; Huang, Horng-chih; Li, Jinglin J.; Miller, Raymond E.; Reitz, David B.; Tremont, Samuel J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 191 pp., Cont.-in-part of U. S. Ser. No. 109,551.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6107494	A	20000822	US 1999-275463	19990324
EP 1440972	A1	20040728	EP 2004-10088	19970311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
US 5994391	A	19991130	US 1998-109551	19980702
EP 1331225	A1	20030730	EP 2003-5459	19981216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CA 2336315	AA	20000113	CA 1999-2336315	19990629
WO 2000001687	A1	20000113	WO 1999-US12828	19990629
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9948202	A1	20000124	AU 1999-48202	19990629
AU 766957	B2	20031030		
EP 1091953	A1	20010418	EP 1999-931769	19990629
EP 1091953	B1	20031210		
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TR 200100824	T2	20010723	TR 2001-200100824	19990629
BR 9911737	A	20011211	BR 1999-11737	19990629
EE 200100002	A	20020617	EE 2001-2	19990629
JP 2002519418	T2	20020702	JP 2000-558091	19990629
NZ 509621	A	20030829	NZ 1999-509621	19990629
AT 256122	E	20031215	AT 1999-931769	19990629
US 6262277	B1	20010717	US 1999-443403	19991119
AU 761249	B2	20030529	AU 2000-53394	20000816
NO 2001000016	A	20010302	NO 2001-16	20010102
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BG 105206	A	20010928	BG 2001-105206	20010131
US 2002013476	A1	20020131	US 2001-828968	20010409
US 6387924	B2	20020514		
US 2002188119	A1	20021212	US 2002-72600	20020211
US 2003171426	A1	20030911	US 2002-76091	20020215
US 6642268	B2	20031104		
JP 2004203891	A2	20040722	JP 2004-50473	20040225

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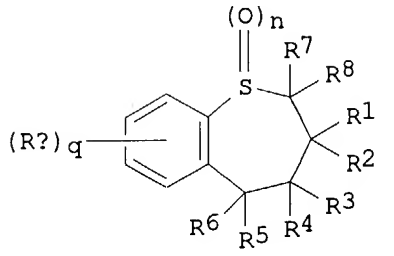
US 1994-305526	B2	19940913
US 1995-517051	B1	19950821
US 1996-13119P	P	19960311
US 1997-816065	B2	19970311
US 1997-831284	B2	19970331
US 1997-68170P	P	19971219
US 1998-109551	A2	19980702

Searcher : Shears 571-272-2528

AU	1997-23266	A3 19970311
EP	1997-915976	A3 19970311
US	1997-40660P	P 19970311
EP	1998-962044	A3 19981216
US	1999-275463	A1 19990324
JP	2000-558091	A3 19990629
WO	1999-US12828	W 19990629
US	1999-443403	A1 19991119
US	2000-676466	A3 20000929
US	2000-581897	A3 20001002

OTHER SOURCE(S): MARPAT 133:193089

GI



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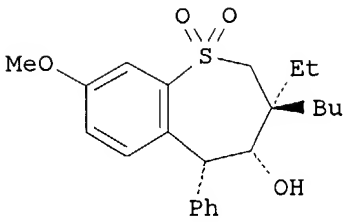

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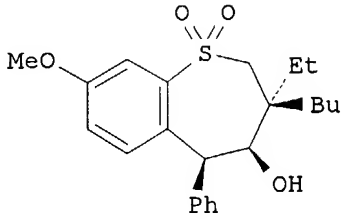


III

AB The title compds. (I) [wherein q = 1-4; n = 2; R1 and R2 = independently H or (un)substituted (halo)alkyl, alkenyl, alkynyl, alkylaryl, arylalkyl, alkoxy(alkyl), dialkylamino, alkylthio, (polyalkyl)aryl, or cycloalkyl; or R1 and R2 taken together with the atoms to which they are attached = cycloalkyl; R3 and R4 = independently H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocyclyl, OR9, NR9R10, SR9, S(O)R9, SO2R9, or SO3R9; R9 and R10 = independently H, (cyclo)alkyl, alkenyl, alkynyl, aryl(alkyl), acyl, heterocyclyl, or ammoniumalkyl; or R3 and R4 together = :O, :NOR11, :S, :NNR11R12, :NR9, or :CR11R12; R11 and R12 = independently H, (cyclo)alkyl, alkenyl, alkynyl, aryl(alkyl), heterocyclyl, carboxylalkyl, carboalkoxyalkyl, cyanoalkyl, OR9, NR9R10, SR9, S(O)R9, SO2R9, SO3R9, CO2R9, CN, halo, oxo, or CONR9R10; R5 = substituted aryl; R6 = H; R7 and R8 = independently H or alkyl; Rx = independently H or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, polyalkyl, acyloxy, aryl(alkyl), halo(alkyl), (quaternary) heterocyclyl, (quaternary) heteroaryl, polyether, alkoxy, amino, alkylthio, NO2, carboxy, carbamido, etc.] where prepared for the prophylaxis and treatment of hyperlipidemic conditions, such as those associated with atherosclerosis or hypercholesterolemia.

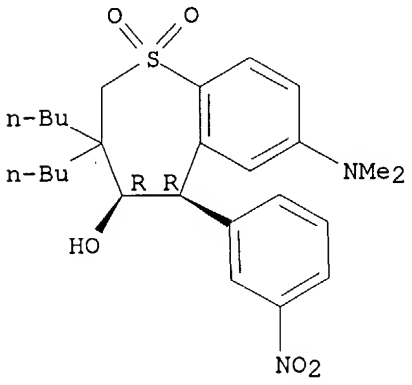
Thus,

KOBu-t was added to a solution of 2-((2-benzyl-5-methoxyphenylsulfonyl)methyl)-2-ethylhexanal (preparation given) and dry THF cooled to -1.6°C to give, after workup, II and III (96% combined yield). The isomers were separated upon recrystn. II inhibited IBAT-mediated uptake of [14C]-taurocholate in H14 cells with an IC50 of 0.1 μM and reduced serum cholesterol from 143 mg (7%) to 126 mg (2%) compared to control in cholesterol-fed hamsters in a 14-day test. In vitro taurocholate uptake assay data are included for nearly 600 compds. of the invention.

IT **197373-50-5P 197373-51-6P 289037-96-3P 289037-98-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

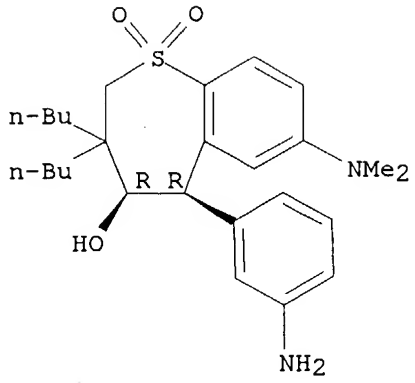
RN 197373-50-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



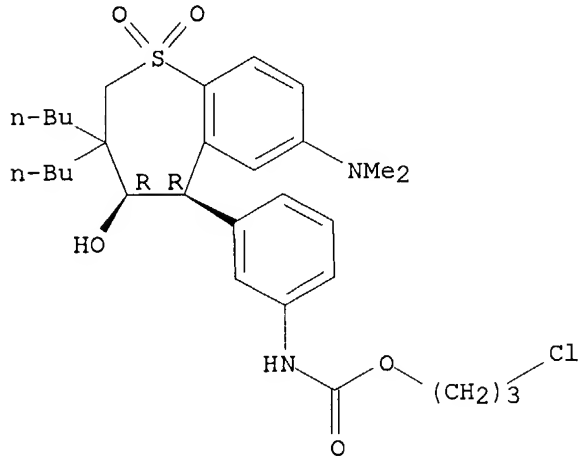
RN 197373-51-6 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



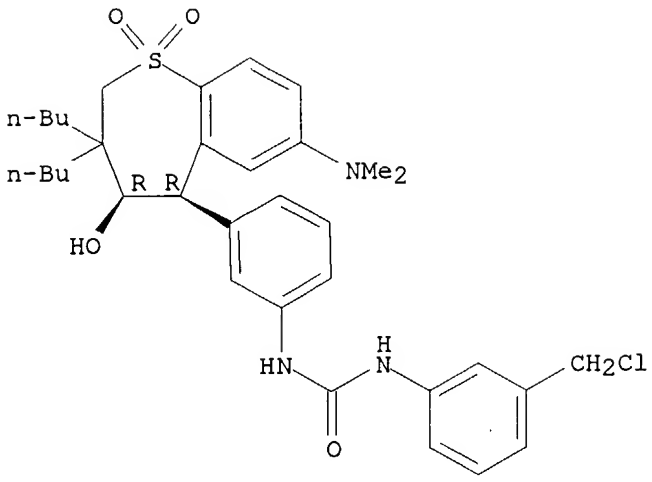
RN 289037-96-3 CAPLUS
CN Carbamic acid, [3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, 3-chloropropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 289037-98-5 CAPLUS
CN Urea, N-[3-(chloromethyl)phenyl]-N'-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

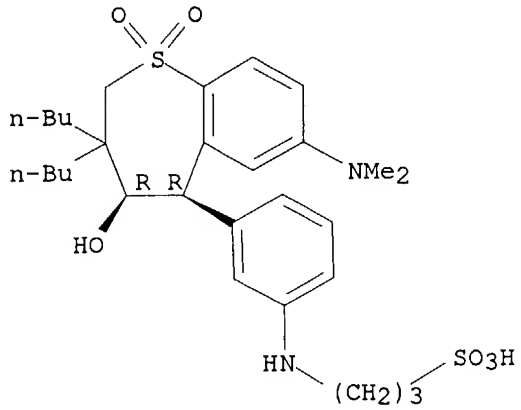


IT **197373-37-8P 197374-04-2P 197374-59-7P**
197375-96-5P 197376-55-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

RN 197373-37-8 CAPLUS

CN 1-Propanesulfonic acid, 3-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-, rel- (9CI) (CA INDEX NAME)

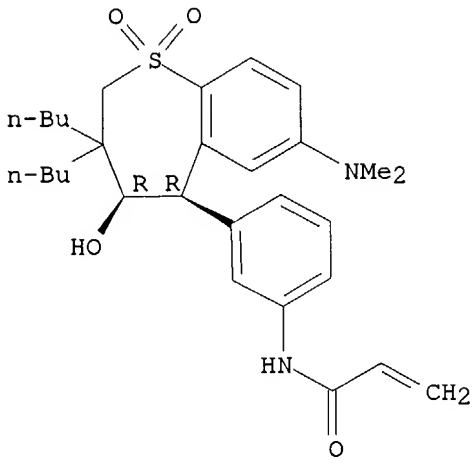
Relative stereochemistry.



RN 197374-04-2 CAPLUS

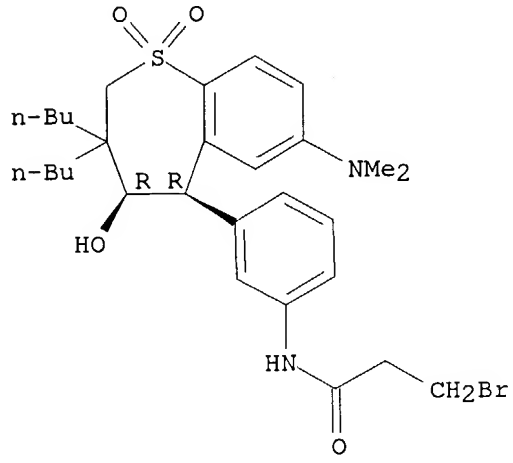
CN 2-Propenamide, N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



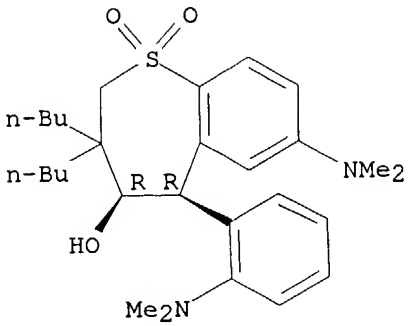
RN 197374-59-7 CAPLUS
CN Propanamide, 3-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



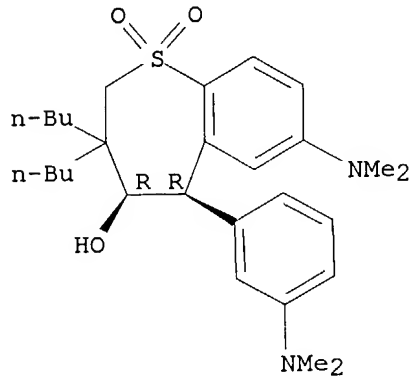
RN 197375-96-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[2-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 197376-55-9 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[3-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:456922 CAPLUS
DOCUMENT NUMBER: 133:94515
TITLE: Combinations for cardiovascular indications
INVENTOR(S): Keller, Bradley T.; Reitz, David B.; Schuh, Joseph R.; Sikorski, James A.; Tremont, Samuel J.; Lappe, Rodney W.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 248 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000038725	A1	20000706	WO 1999-US27946	19991217
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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EP 1140187	A1	20011010	EP 1999-965901	19991217
EP 1140187	B1	20030903		
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BR 9916564	A	20020129	BR 1999-16564	19991217
JP 2002533411	T2	20021008	JP 2000-590676	19991217
EP 1293211	A1	20030319	EP 2002-25631	19991217
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EP 1336413	A1	20030820	EP 2003-9706	19991217
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EP 1340508	A1	20030903	EP 2003-12143	19991217
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EP 1342475	A1	20030910	EP 2003-11146	19991217
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EP 1354604	A1	20031022	EP 2003-16600	19991217
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PT 1140187	T	20040130	PT 1999-965901	19991217
ZA 2001005056	A	20020620	ZA 2001-5056	20010620
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US 2003166720	A1	20030904	US 2002-200600	20020723
US 2003203892	A1	20031030	US 2002-200599	20020723
US 2003109558	A1	20030612	US 2002-245506	20020918
US 2003125316	A1	20030703	US 2002-245507	20020918
US 2004058908	A1	20040325	US 2002-266743	20021009
US 2004029845	A1	20040212	US 2003-373180	20030226
US 2004028644	A1	20040212	US 2003-412694	20030414
US 2004048846	A1	20040311	US 2003-652306	20030902
PRIORITY APPLN. INFO.:			US 1998-113955P	P 19981223

Searcher : Shears 571-272-2528

US 1999-142603P	P	19990707
US 1999-142616P	P	19990707
US 1999-142682P	P	19990707
US 1999-142684P	P	19990707
US 1999-143043P	P	19990707
US 1999-143047P	P	19990707
US 1999-143550P	P	19990713
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EP 1999-965899	A3	19991217
EP 1999-965900	A3	19991217
EP 1999-965901	A3	19991217
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US 1999-465642	A3	19991217
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US 1999-466466	B1	19991217
US 1999-466469	A3	19991217
US 1999-466470	A3	19991217
US 1999-466592	A3	19991217
US 1999-466596	B3	19991217
WO 1999-US27946	W	19991217

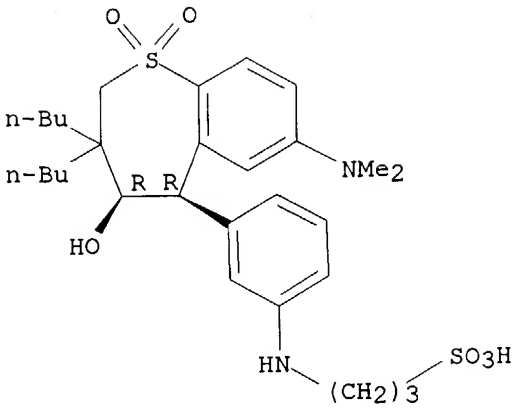
AB The present invention provides combinations of cardiovascular therapeutic compds. for the prophylaxis or treatment of cardiovascular disease including hypercholesterolemia and atherosclerosis. Combinations disclosed include an ileal bile acid transport inhibitor combined with a cholesteryl ester transport protein (CETP) inhibitor, a fibric acid derivative, a nicotinic acid derivative, a microsomal triglyceride transfer protein inhibitor, a cholesterol absorption antagonist, a phytosterol, a stanol, an antihypertensive agent, or others. Further combinations include a CETP inhibitor with a fibric acid derivative, a nicotinic acid derivative, a bile acid sequestrant, a microsomal triglyceride transfer protein inhibitor, a cholesterol absorption antagonist, or others.

IT **197373-37-8D**, enantiomers **280105-90-0D**, enantiomers **280105-98-8D**, enantiomers
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations for cardiovascular agents for treatment of cardiovascular indications)

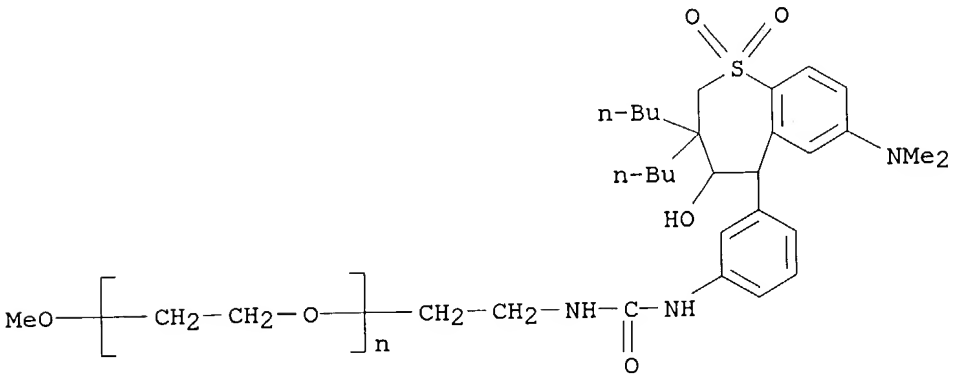
RN 197373-37-8 CAPLUS

CN 1-Propanesulfonic acid, 3-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

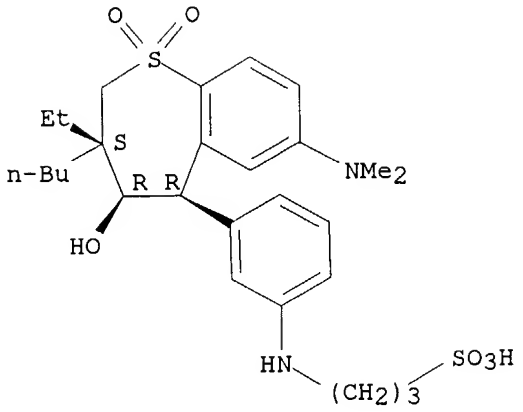


RN 280105-90-0 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]carbonyl]amino]ethyl]-ω-methoxy-, rel- (9CI) (CA INDEX NAME)



RN 280105-98-8 CAPLUS
CN 1-Propanesulfonic acid, 3-[[3-[(3R,4S,5S)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:795803 CAPLUS
DOCUMENT NUMBER: 132:35625
TITLE: Amino acid containing benzo[b]thiepine 1,1-dioxide derivatives as hypolipemic agents
INVENTOR(S): Frick, Wendelin; Enhsen, Alfons; Glombik, Heiner; Heuer, Hubert
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964410	A1	19991216	WO 1999-EP3701	19990528
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19825804	A1	19991216	DE 1998-19825804	19980610
DE 19825804	C2	20000824		
CA 2334775	AA	19991216	CA 1999-2334775	19990528
AU 9945019	A1	19991230	AU 1999-45019	19990528
AU 753275	B2	20021010		
EP 1086092	A1	20010328	EP 1999-927784	19990528
EP 1086092	B1	20021113		
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BR 9912188	A	20010410	BR 1999-12188	19990528

TR 200003634	T2	20010621	TR 2000-200003634		19990528
JP 2002517491	T2	20020618	JP 2000-553419		19990528
AT 227715	E	20021115	AT 1999-927784		19990528
ES 2182535	T3	20030301	ES 1999-927784		19990528
PT 1086092	T	20030331	PT 1999-927784		19990528
RU 2215001	C2	20031027	RU 2001-101491		19990528
TR 200003632	T2	20010420	TR 2000-200003632		19990529
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US 6387944	B1	20020514	US 2000-719047		20001207
US 2002045583	A1	20020418	US 2001-773772		20010202
US 6441022	B2	20020827			
PRIORITY APPLN. INFO.:			DE 1998-19825804	A	19980610
			AU 1997-23266	A3	19970311
			WO 1999-EP3701	W	19990528
			US 1999-398315	A1	19990920

OTHER SOURCE(S): MARPAT 132:35625
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

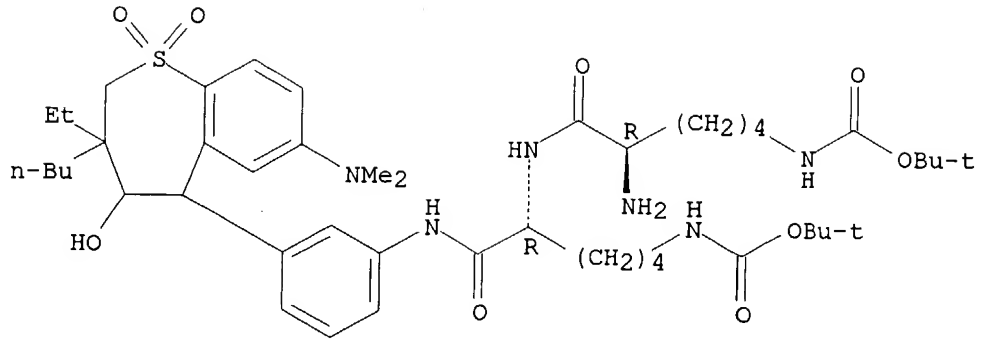
AB Title compds. such as I (mixture of diastereoisomers) were prepared as hypolipemic agents. Thus, I was prepared in 2 sequences from racemic II and Fmoc-D-lys(Boc)-OH, followed by removal of the Fmoc group with Et2NH. I was ≥20 times more active than 3 analogous comparison substances in tests of fecal separation of 14C-taurocholic acid in rats.

IT **252372-02-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(amino acid containing benzo[b]thiepine 1,1-dioxide derivs. as hypolipemic agents)

RN 252372-02-4 CAPLUS

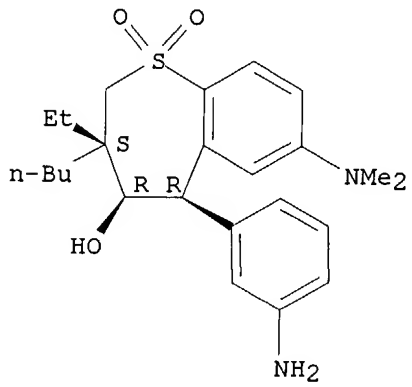
CN D-Lysinamide, N6-[(1,1-dimethylethoxy)carbonyl]-D-lysyl-N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-N6-[(1,1-dimethylethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



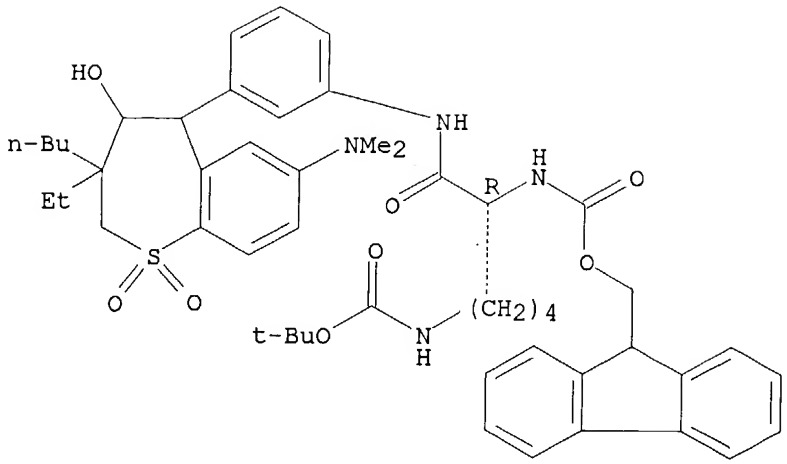
IT **252047-42-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(amino acid containing benzo[b]thiepine 1,1-dioxide derivs. as hypolipemic agents)
RN 252047-42-0 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-, 1,1-dioxide, (3R,4S,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



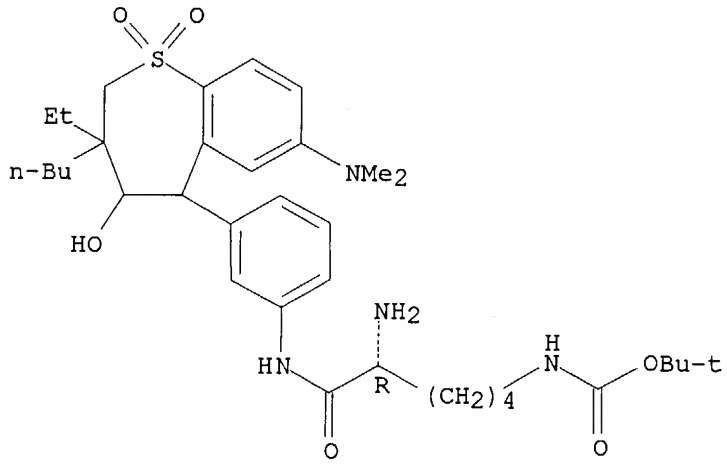
IT **252372-00-2P 252372-01-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid containing benzo[b]thiepine 1,1-dioxide derivs. as hypolipemic agents)
RN 252372-00-2 CAPLUS
CN Carbamic acid, [(1R)-1-[[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]carbonyl]-5-[[(1,1-dimethylethoxy)carbonyl]amino]pentyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 252372-01-3 CAPLUS
CN Carbamic acid, [(5R)-5-amino-6-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-6-oxohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:795802 CAPLUS
DOCUMENT NUMBER: 132:22884
TITLE: Preparation of benzothiepine-1,1-dioxides as hypolipemics
INVENTOR(S): Frick, Wendelin; Enhsen, Alfons; Glombik, Heiner; Heuer, Hubert
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

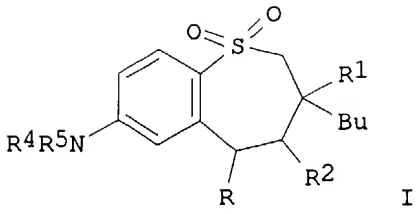
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964409	A2	19991216	WO 1999-EP3743	19990529
WO 9964409	A3	20000302		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19825804	A1	19991216	DE 1998-19825804	19980610
DE 19825804	C2	20000824		
TR 200003634	T2	20010621	TR 2000-200003634	19990528
ES 2182535	T3	20030301	ES 1999-927784	19990528
PT 1086092	T	20030331	PT 1999-927784	19990528
CA 2334773	AA	19991216	CA 1999-2334773	19990529
AU 9945031	A1	19991230	AU 1999-45031	19990529
AU 752633	B2	20020926		
EP 1086113	A2	20010328	EP 1999-927802	19990529
EP 1086113	B1	20040211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
TR 200003632	T2	20010420	TR 2000-200003632	19990529
JP 2002517490	T2	20020618	JP 2000-553418	19990529
JP 3374129	B2	20030204		
NZ 508681	A	20020628	NZ 1999-508681	19990529
RU 2220141	C2	20031227	RU 2001-101499	19990529
AT 259372	E	20040215	AT 1999-927802	19990529
US 6221897	B1	20010424	US 1999-398315	19990920
AU 761249	B2	20030529	AU 2000-53394	20000816
ZA 2000007060	A	20010718	ZA 2000-7060	20001130
ZA 2000007061	A	20010718	ZA 2000-7061	20001130
NO 2000006251	A	20010207	NO 2000-6251	20001208
US 2002045583	A1	20020418	US 2001-773772	20010202
US 6441022	B2	20020827		
US 2003017996	A1	20030123	US 2002-201050	20020724
US 6642269	B2	20031104		
US 2004087648	A1	20040506	US 2003-606771	20030627

PRIORITY APPLN. INFO.:

DE 1998-19825804	A	19980610
US 1996-13119P	P	19960311
AU 1997-23266	A3	19970311
WO 1999-EP3743	W	19990529
US 1999-398315	A1	19990920
US 2001-773772	A1	20010202
US 2002-201050	A1	20020724

OTHER SOURCE(S): MARPAT 132:22884
GI

Searcher : Shears 571-272-2528



I

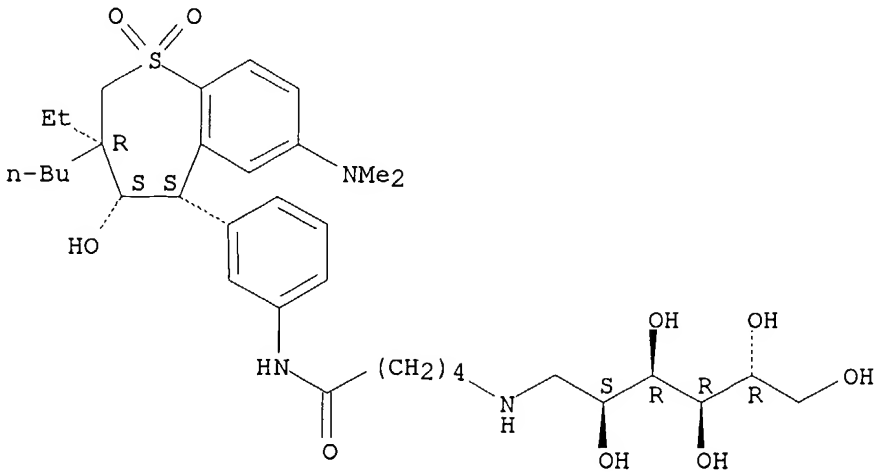
AB Title compds. [I; R = C6H4NHZR3; R1,R4,R5 = Me, Et, Pr, Bu; R2 = H, OH, amino(alkyl); R3 = sugar residue; Z = bond, carbonyl(alkylene), CONH, etc.] were prepared Thus, I [R = C6H4(NHR')-3, R1 = Et, R2 = OH, R4 = R5 = Me](II; R' = H) was amidated by penta-O-acetyl-D-gluconic acid and the product deprotected to give II (R' = gluconoyl) as a mixture of diastereomers. Data for biol. activity of I were given.

IT **252047-36-2P 252047-37-3P 252047-38-4P**
252047-39-5P 252047-40-8P 252047-41-9P
252208-66-5P 252208-67-6P 252208-68-7P
252208-69-8P 252208-70-1P 252208-71-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzothiepine-1,1-dioxides as hypolipemics)

RN 252047-36-2 CAPLUS

CN D-Glucitol, 1-[[5-[[3-[(3R,4S,5S)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]amino]-1-deoxy- (9CI) (CA INDEX NAME)

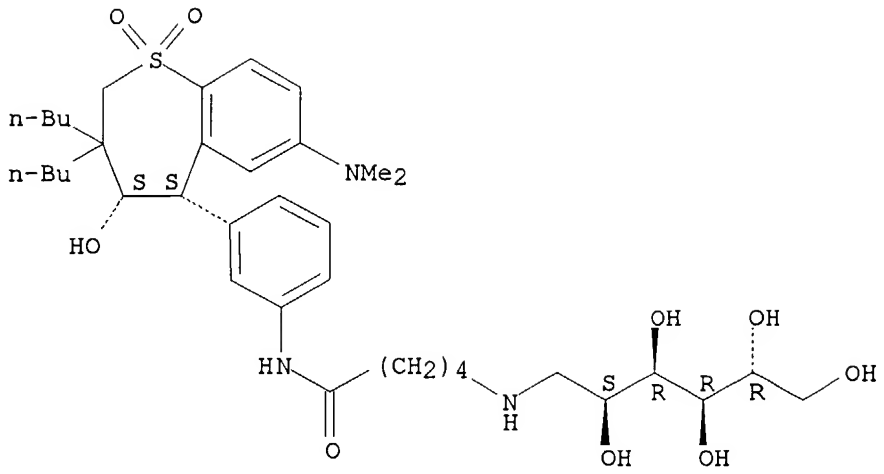
Absolute stereochemistry.



RN 252047-37-3 CAPLUS

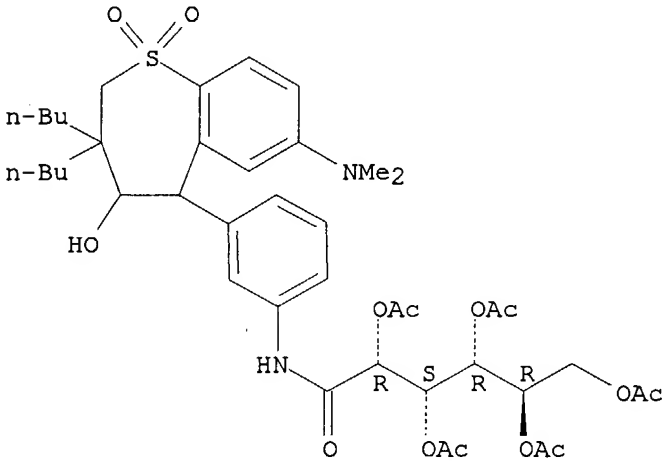
CN D-Glucitol, 1-deoxy-1-[[5-[[3-[(4S,5S)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



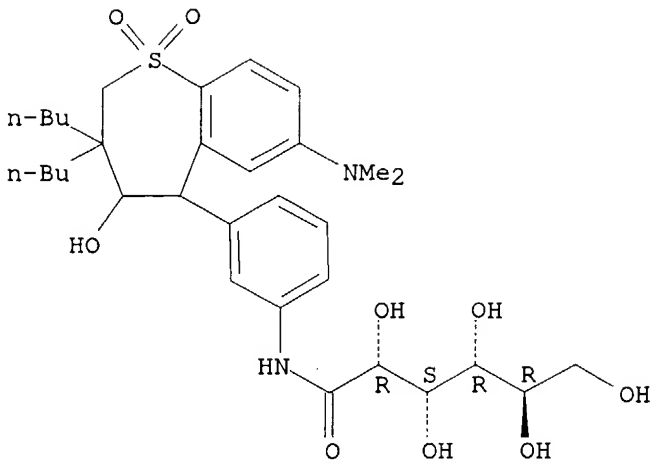
RN 252047-38-4 CAPLUS
CN D-Gluconamide, N-[3-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, 2,3,4,5,6-pentaacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



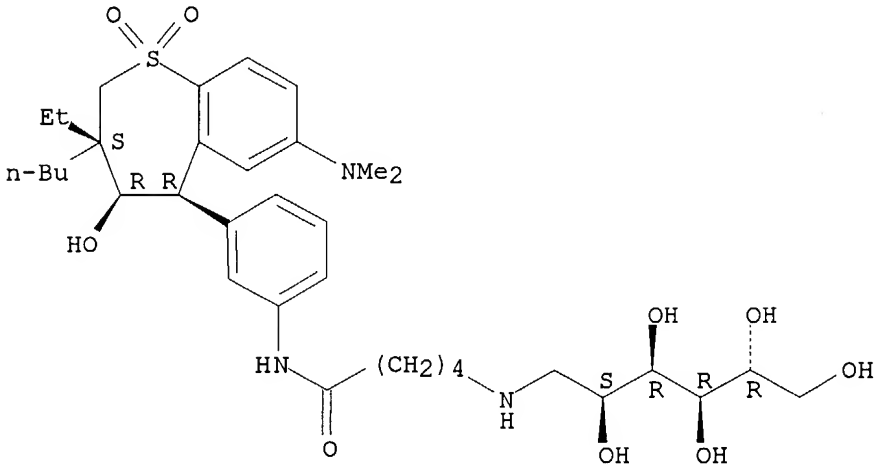
RN 252047-39-5 CAPLUS
CN D-Gluconamide, N-[3-[3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



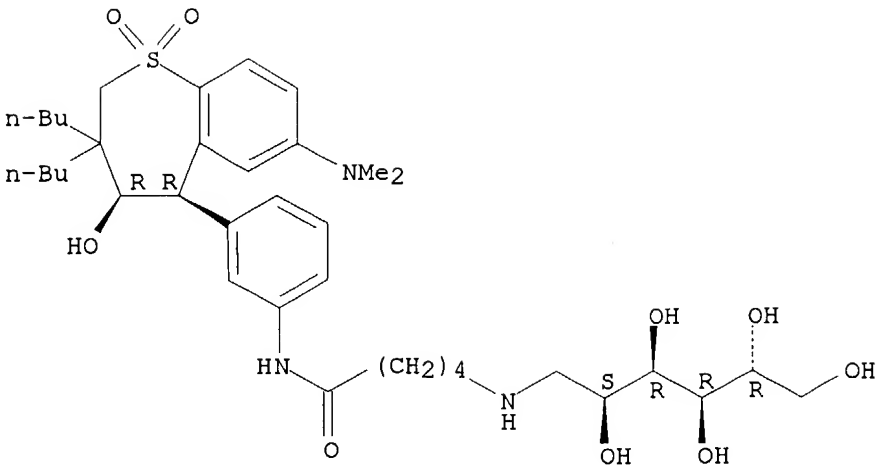
RN 252047-40-8 CAPLUS
CN D-Glucitol, 1-[[5-[[3-[(3S,4R,5R)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]amino]-1-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



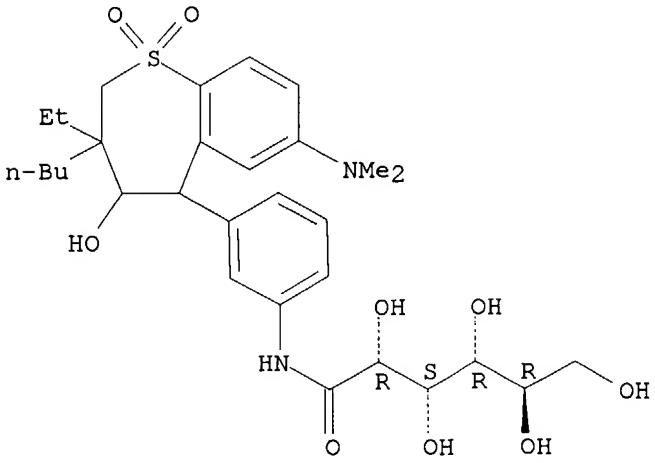
RN 252047-41-9 CAPLUS
CN D-Glucitol, 1-deoxy-1-[[5-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



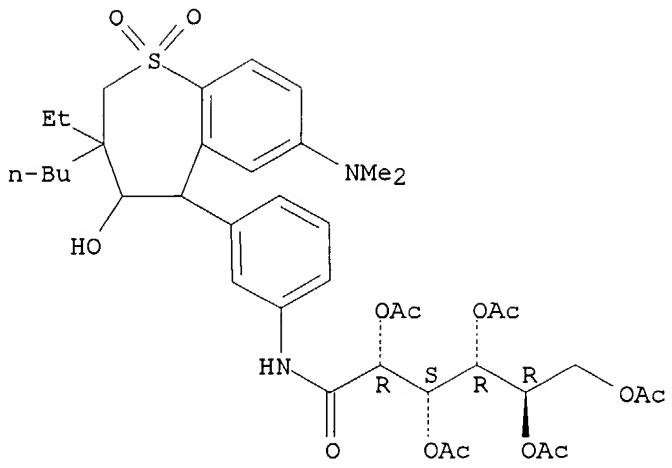
RN 252208-66-5 CAPLUS
CN D-Gluconamide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



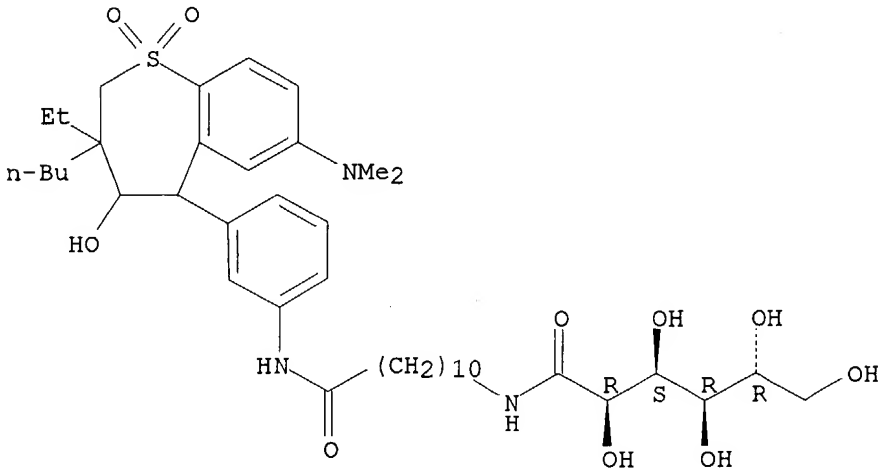
RN 252208-67-6 CAPLUS
CN D-Gluconamide, N-[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, 2,3,4,5,6-pentaacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



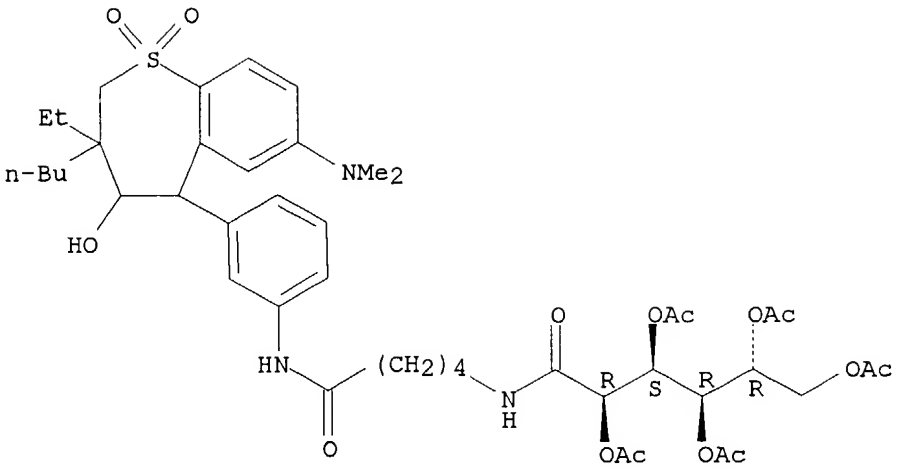
RN 252208-68-7 CAPLUS
CN D-Gluconamide, N-[11-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-11-oxoundecyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



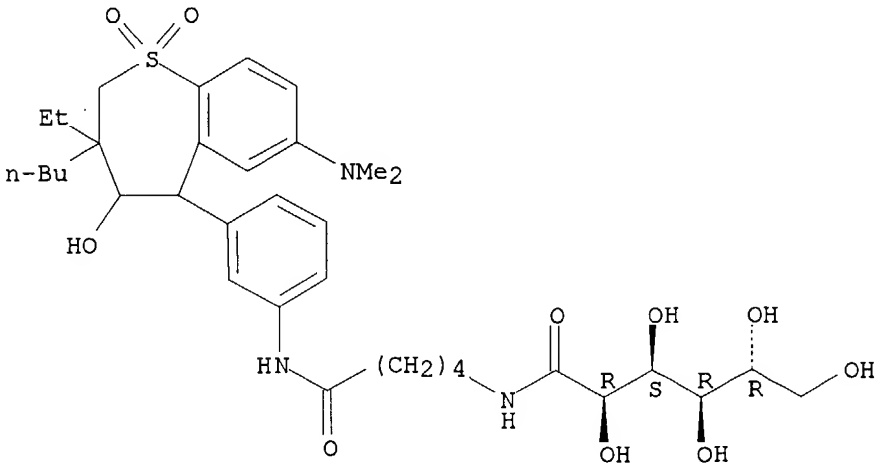
RN 252208-69-8 CAPLUS
CN D-Gluconamide, N-[5-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]-, 2,3,4,5,6-pentaacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



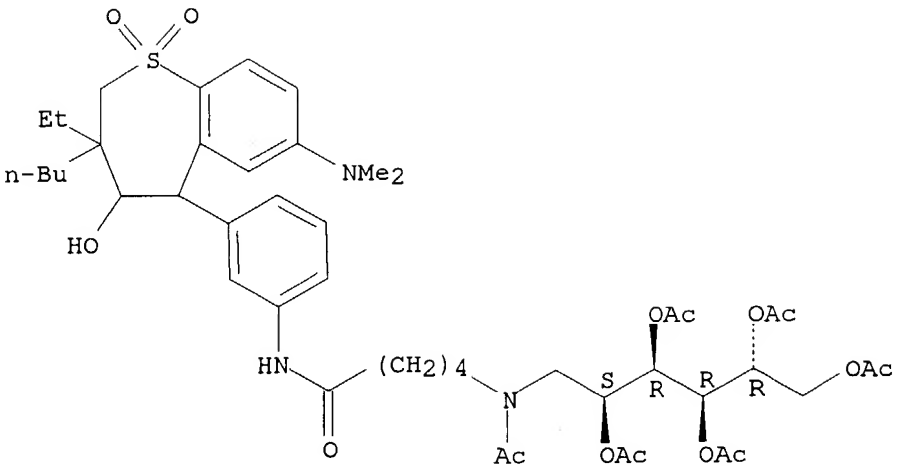
RN 252208-70-1 CAPLUS
CN D-Gluconamide, N-[5-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



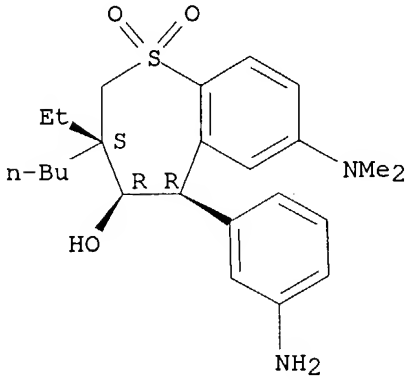
RN 252208-71-2 CAPLUS
CN D-Glucitol, 1-[acetyl[5-[[3-[3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-5-oxopentyl]amino]-1-deoxy-, 2,3,4,5,6-pentaacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



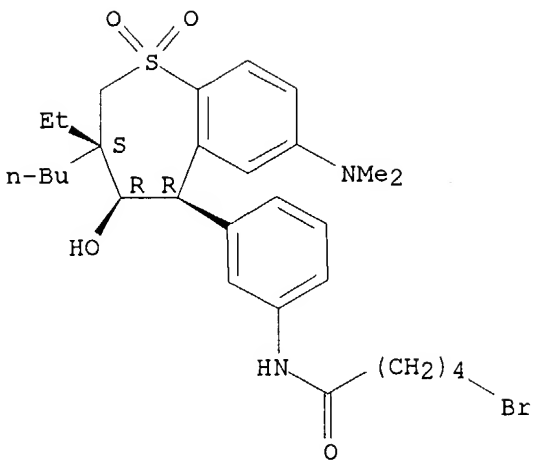
IT **252047-42-0 252047-43-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzothiepine-1,1-dioxides as hypolipemics)
RN 252047-42-0 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-, 1,1-dioxide, (3R,4S,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 252047-43-1 CAPLUS
CN Pentanamide, 5-bromo-N-[3-[(3R,4S,5S)-3-butyl-7-(dimethylamino)-3-ethyl-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L13 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:621210 CAPLUS
DOCUMENT NUMBER: 129:260353
TITLE: Preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors.
INVENTOR(S): Reitz, David B.; Lee, Len F.; Li, Jinglin J.; Huang, Horng-Chih; Tremont, Samuel J.; Miller, Raymond E.; Baneriee, Shyamal C.; Manning, Robert E.; Glenn, Kevin C.; Keller, Bradley T.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; et al.
SOURCE: PCT Int. Appl., 477 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840375	A2	19980917	WO 1998-US3792	19980310
WO 9840375	A3	19981203		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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AU 730024	B2	20010222		
EP 971744	A2	20000119	EP 1998-910075	19980310
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BR 9808013	A	20010925	BR 1998-8013		19980310
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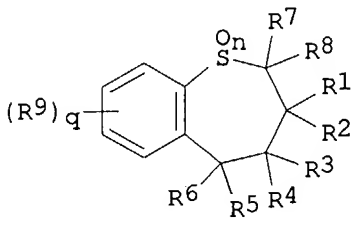
NO 9904390	A	19991104	NO 1999-4390		19990910
AU 761249	B2	20030529	AU 2000-53394		20000816
US 2003171426	A1	20030911	US 2002-76091		20020215
US 6642268	B2	20031104			
PRIORITY APPLN. INFO.:			US 1997-40660P	P	19970311
			US 1994-305526	B2	19940913
			US 1995-517051	B1	19950821
			US 1996-13119P	P	19960311
			AU 1997-23266	A3	19970311
			US 1997-816065	B2	19970311
			US 1997-831284	B3	19970331
			WO 1998-US3792	W	19980310
			US 2000-676466	A3	20000929

OTHER SOURCE(S): MARPAT 129:260353

GI



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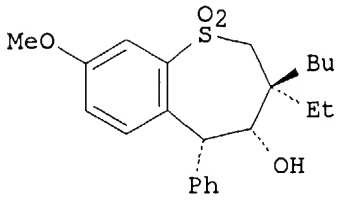


II

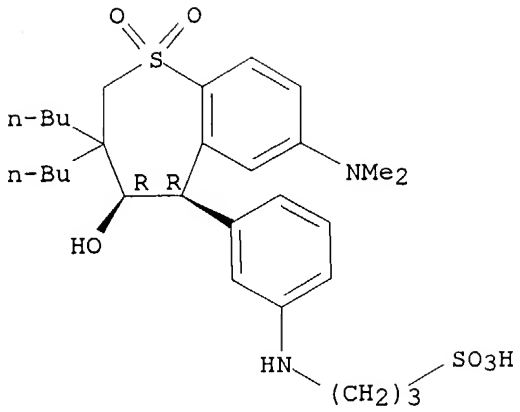
AB Title compds. [I; q = 1-4; n = 0-2; R1, R2 = H, (substituted) alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, alkoxy, dialkylamino, etc.; R1R2C = cycloalkylidene; R3, R4 = H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocyclyl, heteroaryl, etc.; R3R4 = O, S, NOR11, etc.; R11 = H, alkyl, alkenyl, alkynyl, aryl, aralkyl, etc.; R5, R6 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, etc.; R7, R8 = H, alkyl; R9 = H, alkyl, alkenyl, alkynyl, acyloxy, aryl, aralkyl, halo, etc.], were prepared A composition comprising an ileal bile acid transport inhibitor and an HMG Co-A reductase inhibitor is claimed. Thus, title compound (II) (preparation via 2-mercapto-4-methoxybenzophenone given) at 0.2% as an ileal perfusion in guinea pigs reduced HDL cholesterol from 89 mg% to 76 mg%.

IT **197373-37-8P 197374-04-2P 197374-59-7P**
197375-96-5P 197376-55-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

RN 197373-37-8 CAPLUS

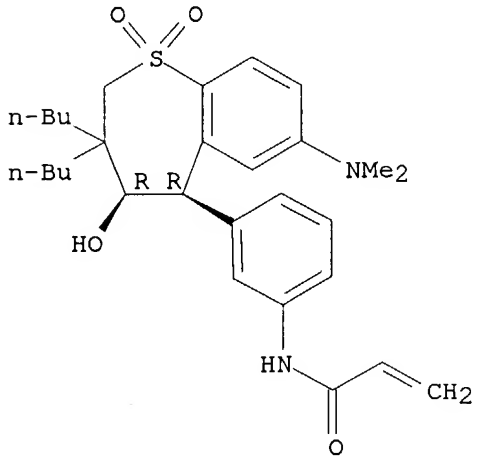
CN 1-Propanesulfonic acid, 3-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



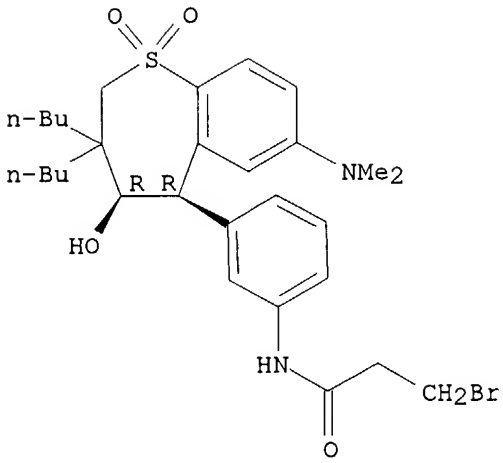
RN 197374-04-2 CAPLUS
CN 2-Propenamide, N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



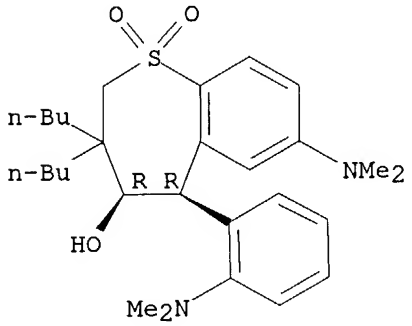
RN 197374-59-7 CAPLUS
CN Propanamide, 3-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



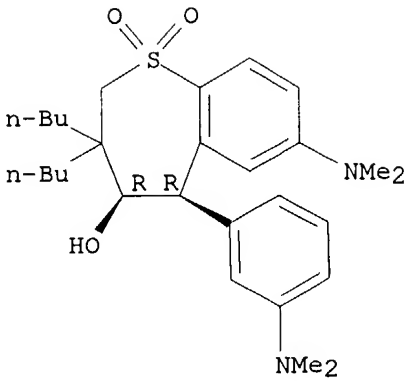
RN 197375-96-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[2-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 197376-55-9 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[3-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

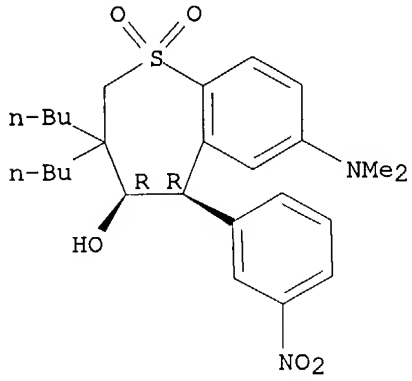
Relative stereochemistry.



IT **197373-50-5P 197373-51-6P 213312-74-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

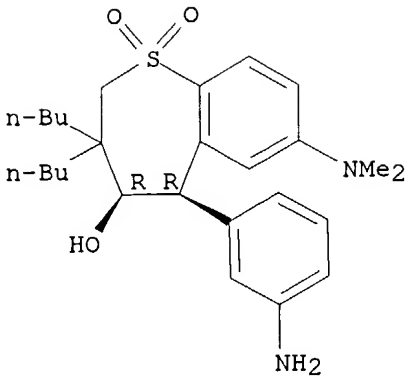
RN 197373-50-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



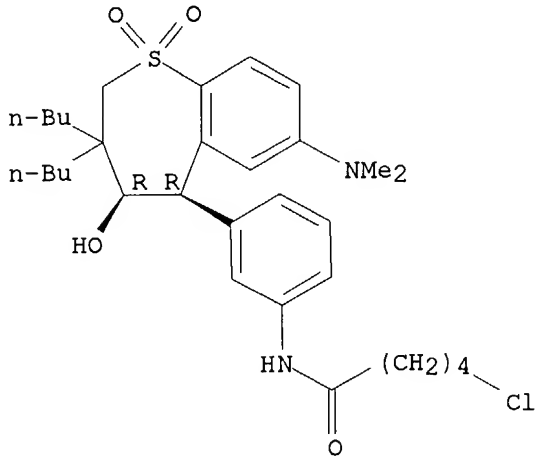
RN 197373-51-6 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 213312-74-4 CAPLUS
CN Pentanamide, 5-chloro-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L13 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:623163 CAPLUS
DOCUMENT NUMBER: 127:307312
TITLE: Novel benzothiepines having activity as inhibitors of ileal bile acid transport and taurocholate uptake
INVENTOR(S): Reitz, David B.; Lee, Len F.; Li, Jinglin J.; Huang, Horng-Chih; Tremont, Samuel J.; Miller, Raymond E.; Banerjee, Shyamal C.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Reitz, David B.; Lee, Len F.; Li, Jinglin J.; Huang, Horng-Chih; Tremont, Samuel J.; Miller, Raymond E.; Banerjee, Shyamal C.
SOURCE: PCT Int. Appl., 406 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733882	A1	19970918	WO 1997-US4076	19970311
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2248586	AA	19970918	CA 1997-2248586	19970311
AU 9723266	A1	19971001	AU 1997-23266	19970311
AU 723123	B2	20000817		
EP 888333	A1	19990107	EP 1997-915976	19970311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1221414	A	19990630	CN 1997-194503	19970311
CN 1110494	B	20030604		
BR 9708042	A	19990727	BR 1997-8042	19970311
JP 2001526627	T2	20011218	JP 1997-532875	19970311
RU 2202549	C2	20030420	RU 1998-118643	19970311
EP 1440972	A1	20040728	EP 2004-10088	19970311
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NO 9804146	A	19981030	NO 1998-4146	19980909
AU 761249	B2	20030529	AU 2000-53394	20000816
US 2003171426	A1	20030911	US 2002-76091	20020215
US 6642268	B2	20031104		

PRIORITY APPLN. INFO.:		
US 1996-13119P	P	19960311
US 1997-816065	A	19970311
US 1994-305526	B2	19940913
US 1995-517051	B1	19950821
AU 1997-23266	A3	19970311
EP 1997-915976	A3	19970311
US 1997-40660P	P	19970311
WO 1997-US4076	W	19970311
US 1997-831284	B3	19970331
US 2000-676466	A3	20000929

OTHER SOURCE(S): MARPAT 127:307312
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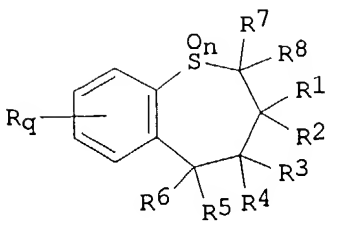

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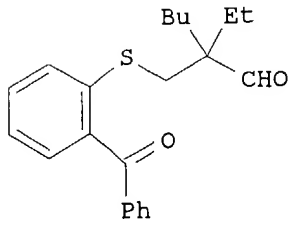
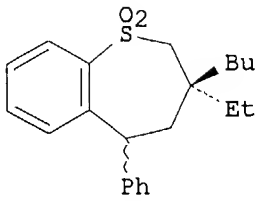


II



III

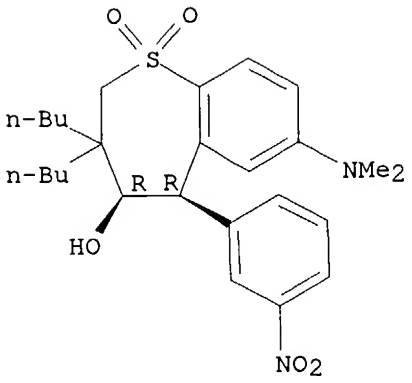
AB Novel benzothiepines I [q = 1-4; n = 0-2; R = H, halo, (un)substituted alk(en/yn)yl, acyloxy, aryl, heterocyclyl, OH or NH2 or SH or derivs., etc.; R1, R2 = H, (un)substituted and/or heteroatom-replaced alk(en/yn)yl, cycloalkyl, aryl, alkoxy, alkylthio, dialkylamino; or CR1R2 = C3-10 cycloalkylidene; R3, R4 = H, alk(en/yn)yl, acyloxy, aryl, heterocyclyl, OH or NH2 or SH or derivs.; or R3R4 = O, S, NH, NOH, NNH2, CH2 or derivs.; R5, R6 = H, (un)substituted alk(en/yn)yl, cycloalkyl, aryl, heterocyclyl, OH or SH or derivs.; R7, R8 = H, alkyl] and their derivs. and analogs are provided. Also provided are pharmaceutical compns. containing I and methods of their medical use, particularly in the prophylaxis and treatment of hyperlipidemic conditions, such as those associated with atherosclerosis or hypercholesterolemia. For instance, the keto aldehyde II was cyclized by Zn/TiCl3, and the resultant cycloolefin was oxidized and epoxidized by m-ClC6H4C(O)OOH and hydrogenated over Pd/C to give epimeric title compds. α- and β-III in 25% and 13% yield, plus addnl. compds. In a test for inhibition of IBAT-mediated uptake of [14C]-taurocholate in H14 cells in vitro, β-III had an IC50 of 5 μM.

IT **197373-50-5P 197373-51-6P 197373-52-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of benzothiepines as antihyperlipidemics)

RN 197373-50-5 CAPLUS

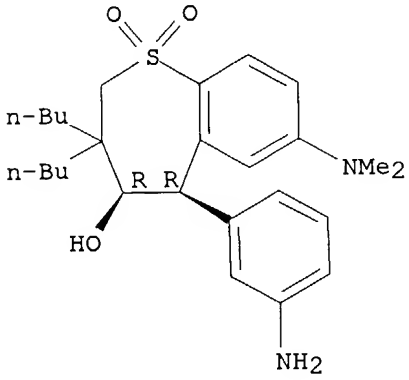
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



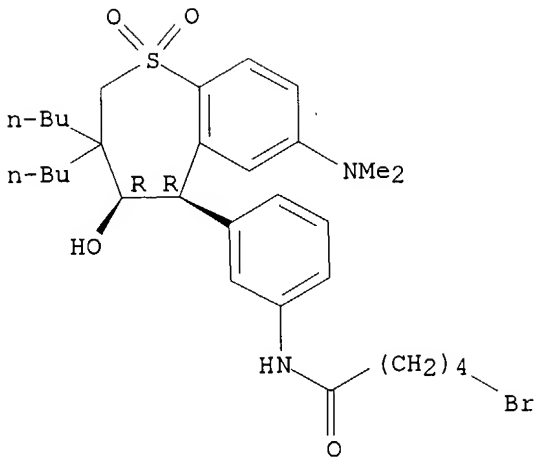
RN 197373-51-6 CAPLUS
CN 1-Benzothiepin-4-ol, 5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 197373-52-7 CAPLUS
CN Pentanamide, 5-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

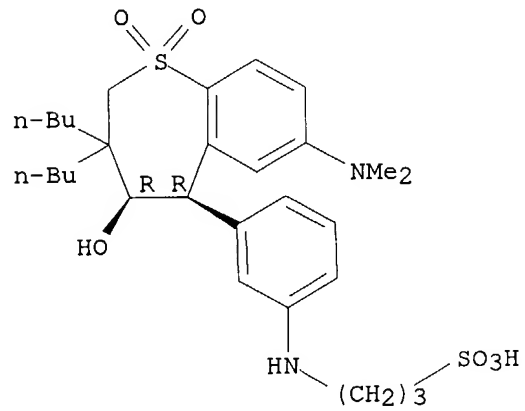


IT **197373-37-8P 197374-04-2P 197374-59-7P**
197375-96-5P 197376-55-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzothiepines as antihyperlipidemics)

RN 197373-37-8 CAPLUS

CN 1-Propanesulfonic acid, 3-[[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]amino]-, rel- (9CI) (CA INDEX NAME)

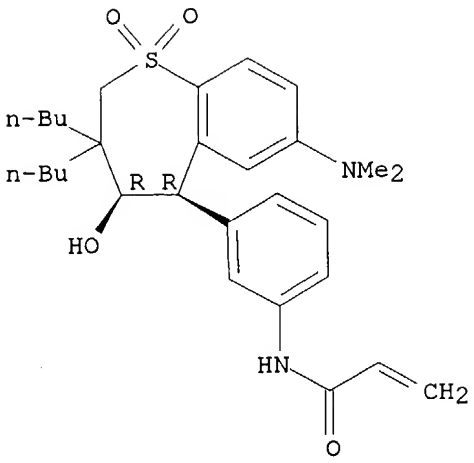
Relative stereochemistry.



RN 197374-04-2 CAPLUS

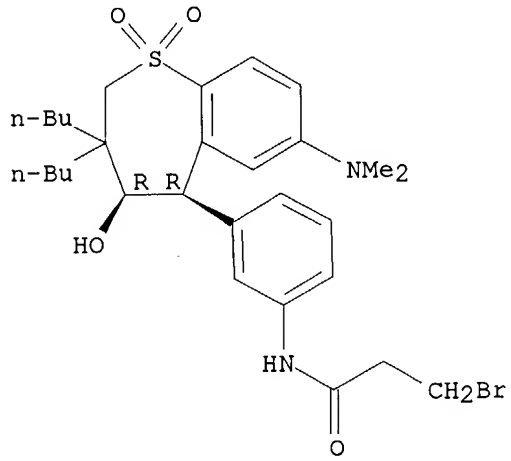
CN 2-Propenamide, N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



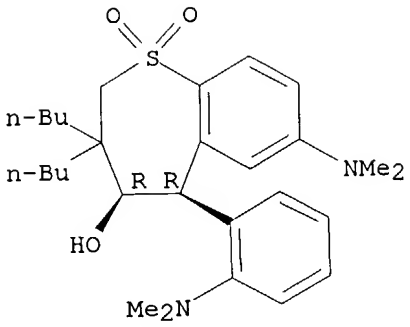
RN 197374-59-7 CAPLUS
CN Propanamide, 3-bromo-N-[3-[(4R,5R)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



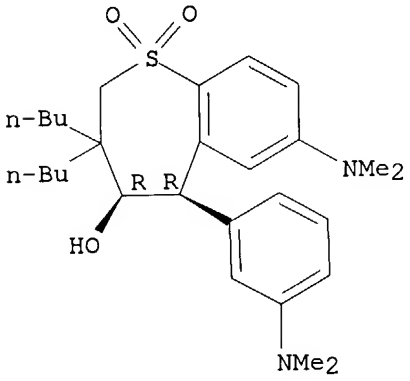
RN 197375-96-5 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[2-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 197376-55-9 CAPLUS
CN 1-Benzothiepin-4-ol, 3,3-dibutyl-7-(dimethylamino)-5-[3-(dimethylamino)phenyl]-2,3,4,5-tetrahydro-, 1,1-dioxide, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



FILE 'CAOLD' ENTERED AT 09:31:14 ON 26 AUG 2004
L14 0 S L12

(FILE 'USPATFULL' ENTERED AT 09:31:19 ON 26 AUG 2004)
L15 12 S L12

L15 ANSWER 1 OF 12 USPATFULL on STN

ACCESSION NUMBER:	2004:204023 USPATFULL
TITLE:	Combination therapy employing ileal bile acid transport inhibiting benzothiepines and HMG Co-A reductase inhibitors
INVENTOR(S):	Keller, Bradley T., Chesterfield, MO, UNITED STATES Glenn, Kevin C., Maryland Heights, MO, UNITED STATES Manning, Robert E., St. Louis, MO, UNITED STATES
PATENT ASSIGNEE(S):	G.D. Searle & Co., Chicago, IL, UNITED STATES, 60680 (U.S. corporation)

PATENT INFORMATION:	NUMBER	KIND	DATE
	US 2004157915	A1	20040812

APPLICATION INFO.: US 2003-620460 A1 20030717 (10)
RELATED APPLN. INFO.: Continuation of Ser. No. US 2002-76091, filed on 15 Feb 2002, GRANTED, Pat. No. US 6642268 Division of Ser. No. US 2000-676466, filed on 29 Sep 2000, GRANTED, Pat. No. US 6420417 Division of Ser. No. US 1998-37308, filed on 9 Mar 1998, GRANTED, Pat. No. US 6268392 Continuation-in-part of Ser. No. US 1997-831284, filed on 31 Mar 1997, ABANDONED Continuation of Ser. No. US 1995-517051, filed on 21 Aug 1995, ABANDONED Continuation-in-part of Ser. No. US 1994-305526, filed on 13 Sep 1994, ABANDONED Continuation-in-part of Ser. No. US 1997-816065, filed on 11 Mar 1997, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-40660P	19970311 (60)
	US 1996-13119P	19960311 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001

NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 6892
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided are novel benzothiepines, derivatives, and analogs thereof; pharmaceutical compositions containing them; and methods of using these compounds and compositions in medicine, particularly in the prophylaxis and treatment of hyperlipidemic conditions such as those associated with atherosclerosis or hypercholesterolemia, in mammals. Also provided are compositions and methods for combination therapy employing ileal bile acid transport inhibitors and HMG Co-A reductase inhibitors for the treatment of hyperlipidemic conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 2 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2004:178975 USPATFULL
TITLE: Application of intestinal biliary acid reuptake inhibitors for the prevention and treatment of alzheimer's disease
INVENTOR(S): Canton, Thierry, Etrechy, FRANCE
Pradier, Laurent, Verrieres, FRANCE
Benavides, Jesus, Chatenay Malabry, FRANCE
Heuer, Hubert, Schwabenheim, GERMANY, FEDERAL REPUBLIC OF
Schaefer, Hans-Ludwig, Hochheim, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): Aventis Pharma S.A., Antony, FRANCE (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004138145	A1	20040715	
APPLICATION INFO.:	US 2003-734787	A1	20031212	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	FR 2002-15722	20021212
	US 2003-455354P	20030317 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROSS J. OEHLER, AVENTIS PHARMACEUTICALS INC., ROUTE 202-206, MAIL CODE: D303A, BRIDGEWATER, NJ, 08807

NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 682
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The subject of the invention is the application of intestinal biliary acid reuptake inhibitors for the prevention and treatment of Alzheimer's disease, where appropriate, in combination with an HMG-CoA reductase inhibitor, a cholesterol uptake inhibitor, a cholesterol synthesis inhibitor or an APP secretase inhibitor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 3 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2004:145088 USPATFULL
TITLE: Combination therapy for the prophylaxis and treatment of hyperlipidemic conditions and disorders
INVENTOR(S): Keller, Bradley T., Chesterfield, MO, UNITED STATES
Tremont, Samuel J., St. Louis, MO, UNITED STATES
Glenn, Kevin C., Maryland Heights, MO, UNITED STATES
Manning, Robert E., St. Louis, MO, UNITED STATES
PATENT ASSIGNEE(S): G.D. SEARLE LLC, Chicago, IL, 60680 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004110761	A1	20040610
APPLICATION INFO.:	US 2003-611942	A1	20030703 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-802313, filed on 8 Mar 2001, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-188378P	20000310 (60)
	US 2000-188361P	20000310 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001

NUMBER OF CLAIMS: 89
EXEMPLARY CLAIM: 1
LINE COUNT: 4655
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel methods and combinations for the treatment and/or prophylaxis of a hyperlipidernic condition or disorder in a subject, wherein the methods comprise the administration of one or more HMG Co-A reductase inhibitors and one or more ASBT inhibitors selected from the specific group of compounds described herein, and the combinations comprise one or more HMG Co-A reductase inhibitors and one or more of said apical sodium

co-dependent bile acid transport inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 4 OF 12 USPATFULL on STN

ACCESSION NUMBER:	2004:108245 USPATFULL
TITLE:	Method for the preparation of tetrahydrobenzothiepines
INVENTOR(S):	Babiak, Kevin A., Evanston, IL, UNITED STATES Carpenter, Andrew, Zebulon, NC, UNITED STATES Chou, Shine, St. Louis, MO, UNITED STATES Colson, Pierre-Jean, Skokie, IL, UNITED STATES Farid, Payman, Vernon Hills, IL, UNITED STATES Hett, Robert, Aarau, SWITZERLAND Huber, Christian H., Skokie, IL, UNITED STATES Koeller, Kevin J., Maryland Heights, MO, UNITED STATES Lawson, Jon P., Glencoe, MO, UNITED STATES Li, James, Pennington, NJ, UNITED STATES Mar, Eduardo K., Northbrook, IL, UNITED STATES Miller, Lawrence M., Des Plaines, IL, UNITED STATES Orlovski, Vladislav, Wheeling, IL, UNITED STATES Peterson, James C., Manchester, MO, UNITED STATES Pozzo, Mark J., Chesterfield, MO, UNITED STATES Przybyla, Claire A., Des Plains, IL, UNITED STATES Tremont, Samuel J., St. Louis, MO, UNITED STATES Trivedi, Jay S., Skokie, IL, UNITED STATES Wagner, Grace M., Webster Groves, MO, UNITED STATES Weisenburger, Gerald A., Evanston, IL, UNITED STATES Zhi, Benxin, Newbury Park, CA, UNITED STATES
PATENT ASSIGNEE(S):	G.D. SEARLE, LLC, Chicago, IL (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004082647	A1	20040429
APPLICATION INFO.:	US 2003-419266	A1	20030421 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2001-802279, filed on 8 Mar 2001, GRANTED, Pat. No. US 6586434		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-188361P	20000310 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001
NUMBER OF CLAIMS:	336
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	15 Drawing Page(s)
LINE COUNT:	5427

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Among its several embodiments, the present invention provides an improved process for the preparation of tetrahydrobenzothiepine-1,1-dioxide compounds; the provision of a process for preparing a diastereomeric mixture of tetrahydrobenzothiepine-1,1-dioxide compounds from a single diastereomer of such compounds; the provision of a process for the preparation of 3-bromo-2-substituted propionaldehyde compounds; and the provision of a process for the preparation of

3-thio-2-substituted propionaldehyde compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 5 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2004:88896 USPATFULL
TITLE: Novel mono- and di-fluorinated benzothiepine compouds as inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake
INVENTOR(S): Tremont, Samuel J., St. Louis, MO, UNITED STATES
Koeller, Kevin J., Maryland Heights, MO, UNITED STATES
PATENT ASSIGNEE(S): G.D. SEARLE, LLC, St. Louis, MO, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004067872	A1	20040408	
	US 6740663	B2	20040525	
APPLICATION INFO.:	US 2002-286987	A1	20021104	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-330892P	20011102 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001
NUMBER OF CLAIMS: 150
EXEMPLARY CLAIM: 1
LINE COUNT: 13074
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mono-fluorinated and di-fluorinated benzothiepine apical sodium co-dependent bile acid transport (ASBT) inhibitors are disclosed together with methods of making the same, methods of using the same to treat hyperlipidemic conditions as well as pharmaceutical compositions containing the same compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 6 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2004:19499 USPATFULL
TITLE: Novel benzothiepines having activity as inhibitors of lleal bile acid transport and taurocholate uptake
INVENTOR(S): Lee, Len F., St. Charles, MO, UNITED STATES
Banerjee, Shyamal C., Chesterfield, MO, UNITED STATES
Huang, Horng-Chih, Chesterfield, MO, UNITED STATES
Li, Jinglin J., Chesterfield, MO, UNITED STATES
Miller, Raymond E., Fairview Heights, IL, UNITED STATES
Reitz, David B., Chesterfield, MO, UNITED STATES
Tremont, Samuel J., St. Louis, MO, UNITED STATES
PATENT ASSIGNEE(S): G.D. Searle & Co., Skokie, IL, UNITED STATES, 60067 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004014803	A1	20040122

APPLICATION INFO.: US 2002-68297 A1 20020208 (10)
RELATED APPLN. INFO.: Division of Ser. No. US 2001-828968, filed on 9 Apr 2001, GRANTED, Pat. No. US 6387924 Continuation-in-part of Ser. No. US 2001-816065, filed on 26 Mar 2001, PENDING Continuation-in-part of Ser. No. US 2001-831284, filed on 4 May 2001, PENDING Continuation of Ser. No. US 1995-517051, filed on 21 Aug 1995, ABANDONED Continuation-in-part of Ser. No. US 1994-305526, filed on 13 Sep 1994, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-13119P	19960311 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001
NUMBER OF CLAIMS: 346
EXEMPLARY CLAIM: 1
LINE COUNT: 12747
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided are novel benzothiepines, derivatives, and analogs thereof; pharmaceutical compositions containing them; and methods of using these compounds and compositions in medicine, particularly in the prophylaxis and treatment of hyperlipidemic conditions such as those associated with atherosclerosis or hypercholesterolemia, in mammals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 7 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2003:335528 USPATFULL
TITLE: Method for the preparation of tetrahydrobenzothiepines
INVENTOR(S): Babiak, Kevin A., Evanston, IL, UNITED STATES
Carpenter, Andrew, Zebulon, NC, UNITED STATES
Chou, Shine, St. Louis, MO, UNITED STATES
Colson, Pierre-Jean, Skokie, IL, UNITED STATES
Farid, Payman, Vernon Hills, IL, UNITED STATES
Hett, Robert, Aarau, SWITZERLAND
Huber, Christian H., Skokie, IL, UNITED STATES
Koeller, Kevin J., Richmond Heights, MD, UNITED STATES
Lawson, Jon P., Glencoe, MO, UNITED STATES
Li, James, Hopewell Township, NJ, UNITED STATES
Mar, Eduardo K., Northbrook, IL, UNITED STATES
Miller, Lawrence M., Des Plaines, IL, UNITED STATES
Orlovski, Vladislav, Wheeling, IL, UNITED STATES
Peterson, James C., Manchester, MO, UNITED STATES
Pozzo, Mark J., Chesterfield, MO, UNITED STATES
Przybyla, Claire A., Des Plaines, IL, UNITED STATES
Tremont, Samuel J., St. Louis, MO, UNITED STATES
Trivedi, Jay S., Skokie, IL, UNITED STATES
Wagner, Grace M., Webster Groves, MO, UNITED STATES
Weisenburger, Gerald A., Des Plaines, IL, UNITED STATES
Zhi, Benxin, Hoffman Estates, IL, UNITED STATES

NUMBER	KIND	DATE

PATENT INFORMATION:	US 2003236406	A1	20031225	
APPLICATION INFO.:	US 2002-204826	A1	20021223	(10)
	WO 2001-US7421		20010308	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Banner & Witcoff, Eleventh Floor, 1001 G Street NW, Washington, DC, 20001-4597
NUMBER OF CLAIMS: 336
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 5434
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Among its several embodiments, the present invention provides an improved process for the preparation of tetrahydrobenzothiepine-1,1-dioxide compounds; the provision of a process for preparing a diastereomeric mixture of tetrahydrobenzothiepine-1,1-dioxide compounds from a single diastereomer of such compounds; the provision of a process for the preparation of 3-bromo-2-substituted propionaldehyde compounds; and the provision of a process for the preparation of 3-thio-2-substituted propionaldehyde compounds. ##STR1## ##STR2##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 8 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2003:330619 USPATFULL
TITLE: Combination therapy for the prophylaxis and treatment of hyperlipidemic conditions and disorders
INVENTOR(S): Keller, Bradley T, Chesterfield, MO, UNITED STATES
Tremont, Samuel J, St Louis, MO, UNITED STATES
Glenn, Kevin C, Maryland Heights, MO, UNITED STATES
Manning, Robert E, St Louis, MO, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003232834	A1	20031218	
APPLICATION INFO.:	US 2002-204672	A1	20021126	(10)
	WO 2001-US7505		20010308	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001
NUMBER OF CLAIMS: 89
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 4647
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of treatment of a host with a cellular proliferative disease, comprising contacting the host with a cephalotaxine and an antiproliferative agent, each in an amount sufficient to modulate said cellular proliferative disease, is described. In some embodiments, the cephalotaxine comprises homoharringtonine (cephalotaxine, 4-methyl-2-hydroxy-2-(4-hydroxy-4-methyl pentyl) butanediocate ester). Antiproliferative agents of the invention comprise alkylating agents, intercalating agents, metal coordination complexes, pyrimidine nucleosides, purine nucleosides, inhibitors of nucleic acid associated enzymes and proteins, and agents affecting structural proteins and

cytoplasmic enzymes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 9 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2002:119900 USPATFULL
TITLE: Combination therapy for the prophylaxis and treatment of hyperlipidemic conditions and disorders
INVENTOR(S): Keller, Bradley T., Chesterfield, MO, UNITED STATES
Tremont, Samuel J., St. Louis, MO, UNITED STATES
Glenn, Kevin C., Maryland Heights, MO, UNITED STATES
Manning, Robert E., St. Louis, MO, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002061888	A1	20020523	
APPLICATION INFO.:	US 2001-802313	A1	20010308	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-188378P	20000310	(60)
	US 2000-188361P	20000310	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001
NUMBER OF CLAIMS: 89
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 4626
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel methods and combinations for the treatment and/or prophylaxis of a hyperlipidemic condition or disorder in a subject, wherein the methods comprise the administration of one or more HMG Co-A reductase inhibitors and one or more ASBT inhibitors selected from the specific group of compounds described herein, and the combinations comprise one or more MIG Co-A reductase inhibitors and one or more of said apical sodium co-dependent bile acid transport inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 10 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2002:55165 USPATFULL
TITLE: Method for the preparation of tetrahydrobenzothiepines
INVENTOR(S): Babiak, Kevin A., Evanston, IL, UNITED STATES
Carpenter, Andrew, Zebulon, NC, UNITED STATES
Chou, Shine, St. Louis, MO, UNITED STATES
Colson, Pierre-Jean, Skokie, IL, UNITED STATES
Farid, Payman, Vernon Hills, IL, UNITED STATES
Hett, Robert, Aarau, SWITZERLAND
Huber, Christian H., Skokie, IL, UNITED STATES
Koeller, Kevin J., Maryland Heights, MO, UNITED STATES
Lawson, Jon P., Glencoe, MO, UNITED STATES
Li, James, Pennington, NJ, UNITED STATES
Mar, Eduardo K., Northbrook, IL, UNITED STATES
Miller, Lawrence M., Des Plaines, IL, UNITED STATES

Orlovski, Vladislav, Wheeling, IL, UNITED STATES
Peterson, James C., Manchester, MO, UNITED STATES
Pozzo, Mark J., Chesterfield, MO, UNITED STATES
Przybyla, Claire A., Des Plaines, IL, UNITED STATES
Tremont, Samuel J., St. Louis, MO, UNITED STATES
Trivedi, Jay S., Skokie, IL, UNITED STATES
Wagner, Grace M., Webster Groves, MO, UNITED STATES
Weisenburger, Gerald A., Evanston, IL, UNITED STATES
Zhi, Benxin, Newbury Park, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002032329	A1	20020314	
	US 6586434	B2	20030701	
APPLICATION INFO.:	US 2001-802279	A1	20010308	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-188361P	20000310 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001
NUMBER OF CLAIMS: 336
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 5437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Among its several embodiments, the present invention provides an improved process for the preparation of tetrahydrobenzothiepine-1,1-dioxide compounds; the provision of a process for preparing a diastereomeric mixture of tetrahydrobenzothiepine-1,1-dioxide compounds from a single diastereomer of such compounds; the provision of a process for the preparation of 3-bromo-2-substituted propionaldehyde compounds; and the provision of a process for the preparation of 3-thio-2-substituted propionaldehyde compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 11 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2001:121499 USPATFULL
TITLE: Combination therapy employing ileal bile acid transport inhibiting benzothiepines and HMG Co-A reductase inhibitors
INVENTOR(S): Keller, Bradley T., Chesterfield, MO, United States
Glenn, Kevin C., Maryland Heights, MO, United States
Manning, Robert E., St. Louis, MO, United States
PATENT ASSIGNEE(S): G. D. Searle & Co., Skokie, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6268392	B1	20010731	
APPLICATION INFO.:	US 1998-37308		19980309	(9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-831284, filed on 31 Mar 1997, now abandoned Continuation of Ser. No.

US 1995-517051, filed on 21 Aug 1995
Continuation-in-part of Ser. No. US 1994-305526, filed on 12 Sep 1994 Continuation-in-part of Ser. No. US 1997-816065, filed on 11 Mar 1997

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-40660P	19970311 (60)
	US 1996-13119P	19960311 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lambkin, Deborah C.
LEGAL REPRESENTATIVE: Williams, Scott A.
NUMBER OF CLAIMS: 49
EXEMPLARY CLAIM: 1
LINE COUNT: 7970
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided are novel benzothiepines, derivatives, and analogs thereof; pharmaceutical compositions containing them; and methods of using these compounds and compositions in medicine, particularly in the prophylaxis and treatment of hyperlipidemic conditions such as those associated with atherosclerosis or hypercholesterolemia, in mammals. Also provided are compositions and methods for combination therapy employing ileal bile acid transport inhibitors and EG Co-A reductase inhibitors for the treatment of hyperlipidemic conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 12 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2000:109998 USPATFULL
TITLE: Substituted 5-aryl-benzothiepines having activity as inhibitors of ileal bile acid transport and taurocholate uptake

INVENTOR(S): Lee, Len F., St. Charles, MO, United States
Banerjee, Shyamal C., Chesterfield, MO, United States
Huang, Horng-Chih, Chesterfield, MO, United States
Li, Jinglin J., Chesterfield, MO, United States
Miller, Raymond E., Fairview Heights, IL, United States
Reitz, David B., Chesterfield, MO, United States
Tremont, Samuel J., St. Louis, MO, United States
PATENT ASSIGNEE(S): G.D. Searle and Company, Skokie, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6107494		20000822
APPLICATION INFO.:	US 1999-275463		19990324 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-109551, filed on 2 Jul 1998 which is a continuation-in-part of Ser. No. US 1997-816065, filed on 11 Mar 1997, now abandoned And a continuation-in-part of Ser. No. US 1997-831284, filed on 31 Mar 1997, now abandoned which is a continuation of Ser. No. US 1995-517051, filed on 21 Aug 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-305526, filed on 12 Sep 1994, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-13119P	19960311 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lambkin, Deborah C.
LEGAL REPRESENTATIVE: Senniger, Powers, Leavitt & Roedel
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 9643
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided are novel benzothiepines, derivatives, and analogs thereof; pharmaceutical compositions containing them; and methods of using these compounds and compositions in medicine, particularly in the prophylaxis and treatment of hyperlipidemic conditions such as those associated with atherosclerosis or hypercholesterolemia, in mammals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MARPAT' ENTERED AT 09:31:41 ON 26 AUG 2004)

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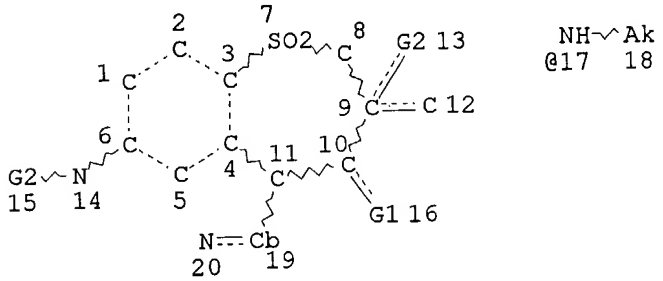

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GGCAT IS UNS AT 19
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L19 13 SEA FILE=MARPAT ABB=ON PLU=ON L18/COMPLETE ← only iterations that are complete

Searcher : Shears 571-272-2528

L19 ANSWER 1 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 141:17641 MARPAT
TITLE: Methods and compositions for the prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors
PATENT ASSIGNEE(S): Aventis Pharma SA, Fr.
SOURCE: Fr. Demande, 25 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2848452	A1	20040618	FR 2002-15722	20021212
WO 2004062652	A1	20040729	WO 2003-FR3654	20031210

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004138145	A1	20040715	US 2003-734787	20031212
			FR 2002-15722	20021212
PRIORITY APPLN. INFO.:			US 2003-455354P	20030317

AB The invention describe the application of the intestinal biliary acid reuptake inhibitors for the prevention and the treatment of Alzheimer's disease, alone or in conjunction with an HMG-CoA reductase inhibitor , a cholesterol uptake inhibitor, a cholesterol synthesis inhibitor or an inhibitor of APP secretases.

IC ICM A61K031-444
ICS A61K031-38; A61P025-28
CC 1-11 (Pharmacology)
ST bile acid reuptake inhibitors intestine Alzheimers disease treatment prevention
IT Intestine
(biliary acid reuptake; methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)
IT Alzheimer's disease
Anti-Alzheimer's agents
Human
(methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)
IT Bile acids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reuptake inhibitors; methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)
IT Biological transport

(reuptake, bile acid, inhibitors of; methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)

IT Biological transport
(uptake, cholesterol, inhibitors of, in conjunction with treatment; methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)

IT 9028-35-7, HMG-CoA reductase 158736-49-3, β-Secretase 338454-52-7, γ Secretase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, in conjunction with treatment; methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)

IT 252047-40-8 263562-55-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)

IT 57-88-5, Cholesterol, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(uptake and synthesis inhibitors, in conjunction with treatment; methods and compns. for prevention and treatment of Alzheimer's disease with intestinal bile acid reuptake inhibitors)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 13 MARPAT COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 140:111291 MARPAT

TITLE: Preparation of substituted 5-aryl-benzothiepines as ileal bile acid transport and taurocholate uptake inhibitors

INVENTOR(S): Lee, Len F.; Banerjee, Shyamal C.; Huang, Horng Chih; Li, Jinglin J.; Miller, Raymond E.; Reitz, David B.; Tremont, Sanuel J.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S. Pat. Appl. Publ., 235 pp., Cont.-in-part of U.S. Ser. No. 831,284.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004014803	A1	20040122	US 2002-68297	20020208
EP 1440972	A1	20040728	EP 2004-10088	19970311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AU 761249	B2	20030529	AU 2000-53394	20000816
US 2002013476	A1	20020131	US 2001-828968	20010409
US 6387924	B2	20020514		
US 2003171426	A1	20030911	US 2002-76091	20020215
US 6642268	B2	20031104		
PRIORITY APPLN. INFO.:			US 1994-305526	19940913

US 1995-517051	19950821
US 1996-13119P	19960311
US 1997-816065	19970311
US 2001-828968	20010409
US 2001-831284	20010504
AU 1997-23266	19970311
EP 1997-915976	19970311
US 1997-40660P	19970311
US 1997-831284	19970331
US 1997-68170P	19971219
US 1998-109551	19980702
US 1999-275463	19990324
US 1999-443403	19991119
US 2000-676466	20000929

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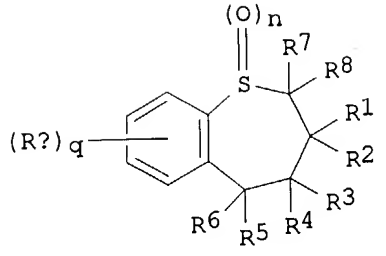

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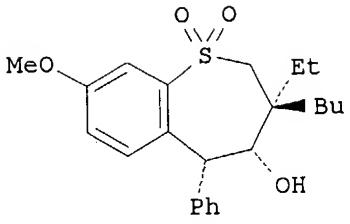

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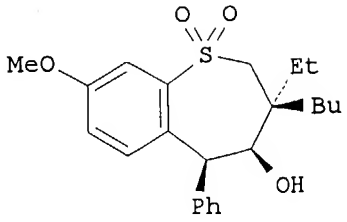


III

AB The title compds. (I) [wherein q = 1-4; n = 0-2; R1, R2 = H, (un)substituted (halo)alkyl, alkenyl, alkynyl, alkylaryl, arylalkyl, alkoxy(alkyl), dialkylamino, alkylthio, (polyalkyl)aryl, or cycloalkyl; or R1 and R2 taken together with the atoms to which they are attached = cycloalkyl; R3, R4 = H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocyclyl, OR9, NR9R10, SR9, S(O)R9, SO2R9, or SO3R9; R9, R10 = H, (cyclo)alkyl, alkenyl, alkynyl, aryl(alkyl), acyl, heterocyclyl, or ammoniumalkyl; or R3 and R4 together = :O, :NOR11, :S, :NNR11R12, :NR9, or :CR11R12; R11, R12 = H, (cyclo)alkyl, alkenyl, alkynyl, aryl(alkyl), heterocyclyl, carboxylalkyl, carboalkoxyalkyl, cyanoalkyl, OR9, NR9R10, SR9, S(O)R9, SO2R9, SO3R9, CO2R9, CN, halo, oxo, or CONR9R10; R5, R6 = H, alkyl, aryl, etc.; R7, R8 = H, alkyl; Rx = H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, polyalkyl, acyloxy, aryl(alkyl), halo(alkyl), (quaternary) heterocyclyl, (quaternary) heteroaryl, polyether, alkoxy, amino, alkylthio, NO2, carboxy, carbamido, etc.] were prepared for the prophylaxis and treatment of hyperlipidemic conditions, such as those associated with atherosclerosis or hypercholesterolemia. Thus,

KOBu-t was added to a solution of 2-((2-benzyl-5-methoxyphenylsulfonyl)methyl)-2-ethylhexanal (preparation given) and dry THF cooled to -1.6°C to give, after workup, II and III (96% combined yield). The isomers were separated upon recrystn. II inhibited IBAT-mediated uptake of [14C]-taurocholate in H14 cells with an IC50 of 0.1 μM and reduced serum cholesterol from 143 mg (7%) to 126 mg (2%) compared to control in cholesterol-fed hamsters in a 14-day test. In vitro taurocholate uptake assay data are included for nearly 600 compds. of the invention.

IC C07D337-16; A61K031-38

NCL 514431000

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

ST arylbenzothiepine prepn ileal bile acid transport inhibitor; benzothiepine prepn taurocholate uptake inhibitor; hypolipemic antiatherosclerotic anticholesterolemic arylbenzothiepine prepn

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia, treatment of; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of ileal; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT Anticholesteremic agents
Human
Hypolipemic agents
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT Atherosclerosis
Hypercholesterolemia
(treatment of; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 178678-22-3P 178678-23-4P 178678-24-5P 178678-25-6P 178678-26-7P
178678-27-8P 178678-29-0P 178678-33-6P 178678-34-7P 178678-37-0P
178678-46-1P 178678-49-4P 178678-50-7P 178678-51-8P 178678-57-4P
178678-58-5P 178678-59-6P 178897-97-7P 178897-98-8P 178898-00-5P
178898-05-0P 197372-67-1P 197372-71-7P 197372-76-2P 197372-77-3P
197372-78-4P 197373-42-5P 197373-43-6P 197373-44-7P 197373-47-0P
197373-49-2P 197373-50-5P 197373-51-6P 197373-55-0P 197373-56-1P
197373-57-2P 197373-58-3P 197375-48-7P 197375-49-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by

cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 178678-28-9P 178678-30-3P 178678-31-4P 178678-35-8P 178678-36-9P
178678-39-2P 178678-40-5P 178678-41-6P 178678-42-7P 178678-43-8P
178678-44-9P 178678-45-0P 178678-47-2P 178678-48-3P 178678-52-9P
178678-53-0P 178678-54-1P 178897-95-5P 178897-96-6P 178897-99-9P
178898-01-6P 178898-02-7P 178898-03-8P 178898-04-9P 197372-66-0P
197372-69-3P 197372-70-6P 197372-72-8P 197372-73-9P 197372-74-0P
197372-75-1P 197372-79-5P 197372-80-8P 197372-81-9P 197372-82-0P
197372-83-1P 197372-84-2P 197372-85-3P 197372-86-4P 197372-87-5P
197372-88-6P 197372-89-7P 197372-90-0P 197372-91-1P 197372-92-2P
197372-93-3P 197372-94-4P 197372-95-5P 197372-96-6P 197372-97-7P
197372-98-8P 197372-99-9P 197373-00-5P 197373-01-6P 197373-02-7P
197373-03-8P 197373-04-9P 197373-05-0P 197373-06-1P 197373-07-2P
197373-08-3P 197373-09-4P 197373-10-7P 197373-11-8P 197373-12-9P
197373-13-0P 197373-14-1P 197373-16-3P 197373-17-4P 197373-18-5P
197373-19-6P 197373-20-9P 197373-22-1P 197373-24-3P 197373-25-4P
197373-26-5P 197373-27-6P 197373-28-7P 197373-29-8P 197373-30-1P
197373-35-6P 197373-36-7P 197373-37-8P 197373-38-9P 197373-39-0P
197373-40-3P 197373-41-4P 197373-45-8P 197373-48-1P 197373-54-9P
197373-59-4P 197373-60-7P 197373-61-8P 197373-62-9P 197373-63-0P
197373-64-1P 197373-66-3P 197373-67-4P 197373-68-5P 197373-69-6P
197373-70-9P 197373-71-0P 197373-72-1P 197373-73-2P 197373-75-4P
197373-76-5P 197373-77-6P 197373-78-7P 197373-79-8P 197373-80-1P
197373-81-2P 197373-83-4P 197373-85-6P 197373-87-8P 197373-90-3P
197373-93-6P 197373-95-8P 197373-97-0P 197373-99-2P 197374-00-8P
197374-01-9P 197374-02-0P 197374-03-1P 197374-04-2P 197374-06-4P
197374-08-6P 197374-09-7P 197374-10-0P 197374-11-1P 197374-13-3P
197374-14-4P 197374-16-6P 197374-17-7P 197374-18-8P 197374-19-9P
197374-20-2P 197374-21-3P 197374-22-4P 197374-24-6P 197374-25-7P
197374-26-8P 197374-27-9P 197374-29-1P 197374-30-4P 197374-31-5P
197374-32-6P 197374-34-8P 197374-35-9P 197374-37-1P 197374-38-2P
197374-39-3P 197374-40-6P 197374-41-7P 197374-43-9P 197374-44-0P
197374-45-1P 197374-46-2P 197374-47-3P 197374-48-4P 197374-49-5P
197374-50-8P 197374-51-9P 197374-52-0P 197374-53-1P 197374-54-2P
197374-55-3P 197374-56-4P 197374-57-5P 197374-58-6P 197374-59-7P
197374-60-0P 197374-62-2P 197374-63-3P 197374-64-4P 197374-65-5P
197374-66-6P 197374-67-7P 197374-68-8P 197374-69-9P 197374-71-3P
197374-72-4P 197374-73-5P 197374-74-6P 197374-75-7P 197374-76-8P
197374-77-9P 197374-78-0P 197374-79-1P 197374-80-4P 197374-81-5P
197374-82-6P 197374-83-7P 197374-84-8P 197374-85-9P 197374-86-0P
197374-87-1P 197374-88-2P 197374-89-3P 197374-90-6P 197374-91-7P
197374-92-8P 197374-93-9P 197374-94-0P 197374-95-1P 197374-96-2P
197374-97-3P 197374-98-4P 197374-99-5P 197375-00-1P 197375-01-2P
197375-02-3P 197375-03-4P 197375-04-5P 197375-05-6P 197375-06-7P
197375-07-8P 197375-08-9P 197375-09-0P 197375-10-3P 197375-11-4P
197375-12-5P 197375-13-6P 197375-14-7P 197375-15-8P 197375-16-9P
197375-17-0P 197375-20-5P 197375-22-7P 197375-23-8P 197375-24-9P
197375-25-0P 197375-26-1P 197375-28-3P 197375-30-7P 197375-32-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 197375-34-1P 197375-39-6P 197375-42-1P 197375-44-3P 197375-52-3P

197375-57-8P 197375-60-3P 197375-63-6P 197375-66-9P 197375-68-1P
197375-70-5P 197375-72-7P 197375-74-9P 197375-75-0P 197375-80-7P
197375-82-9P 197375-84-1P 197375-86-3P 197375-89-6P 197375-93-2P
197375-94-3P 197375-96-5P 197375-98-7P 197376-00-4P 197376-02-6P
197376-04-8P 197376-06-0P 197376-07-1P 197376-08-2P 197376-09-3P
197376-10-6P 197376-11-7P 197376-12-8P 197376-13-9P 197376-14-0P
197376-15-1P 197376-17-3P 197376-18-4P 197376-19-5P 197376-21-9P
197376-22-0P 197376-25-3P 197376-31-1P 197376-32-2P 197376-34-4P
197376-36-6P 197376-38-8P 197376-40-2P 197376-42-4P 197376-46-8P
197376-49-1P 197376-52-6P 197376-55-9P 197376-58-2P 197376-61-7P
197376-64-0P 197376-67-3P 197376-69-5P 197376-73-1P 197376-74-2P
197376-75-3P 197376-76-4P 197376-77-5P 197376-78-6P 197376-79-7P
197376-81-1P 197376-82-2P 197376-83-3P 197376-84-4P 197376-85-5P
197376-86-6P 197376-88-8P 197376-89-9P 197376-90-2P 197376-92-4P
197376-94-6P 197376-95-7P 197376-97-9P 197376-99-1P 197377-00-7P
197377-02-9P 197377-03-0P 197377-05-2P 197377-09-6P 197377-10-9P
197377-11-0P 197377-12-1P 197377-14-3P 197377-16-5P 197377-17-6P
197377-18-7P 197377-19-8P 197377-20-1P 197377-21-2P 197377-22-3P
197377-23-4P 197377-24-5P 197377-25-6P 197377-26-7P 197377-27-8P
197377-28-9P 197377-29-0P 197377-30-3P 197377-31-4P 197377-32-5P
197377-33-6P 197377-34-7P 197377-35-8P 197377-36-9P 197377-37-0P
197377-38-1P 197377-39-2P 197377-40-5P 197377-42-7P 197377-43-8P
197377-45-0P 197377-46-1P 197377-47-2P 197377-48-3P 197377-49-4P
197377-50-7P 197377-51-8P 197377-53-0P 197377-54-1P 197377-55-2P
197377-57-4P 197377-58-5P 197377-60-9P 197377-61-0P 197377-62-1P
197377-63-2P 197377-64-3P 197377-65-4P 197377-66-5P 197377-68-7P
197377-69-8P 197377-70-1P 197377-71-2P 197377-72-3P 197377-73-4P
197377-74-5P 197377-75-6P 197377-76-7P 197377-77-8P 197377-78-9P
197377-79-0P 197377-81-4P 197377-82-5P 197377-83-6P 197377-84-7P
197377-85-8P 197377-86-9P 197377-90-5P 197377-94-9P 197377-96-1P
197377-98-3P 197384-36-4P 197384-39-7P 197390-49-1P 197390-68-4P
213312-50-6P 213312-80-2P 213312-99-3P 213313-15-6P 213313-34-9P
213386-72-2P 228113-66-4P 289037-53-2P 289037-54-3P 289037-55-4P
289037-56-5P 289037-57-6P 289037-58-7P 289037-59-8P 289037-60-1P
289037-61-2P 289037-62-3P 289037-64-5P 289037-65-6P 289037-67-8P
289037-68-9P 289037-70-3P 289037-72-5P 289037-74-7P 289037-75-8P
289037-76-9P 289037-77-0P 289037-78-1P 289037-79-2P 289037-80-5P
289037-81-6P 289037-82-7P 289037-83-8P 289037-84-9P 289037-85-0P
289037-86-1P 289037-87-2P 289037-88-3P 289037-90-7P 289037-91-8P
289037-92-9P 289037-93-0P 289037-94-1P 289037-95-2P 289038-00-2P
289038-01-3P 289038-02-4P 289038-03-5P 289038-04-6P 289038-05-7P
289038-06-8P 289038-07-9P 289038-09-1P 289038-11-5P 289038-13-7P
289038-15-9P 289038-16-0P 289038-18-2P 289038-19-3P 289038-21-7P
289038-23-9P 289038-24-0P 289038-25-1P 289038-26-2P 289038-27-3P
289038-28-4P 289038-29-5P 289038-30-8P 289038-32-0P 289038-33-1P
289038-34-2P 289038-35-3P 289038-36-4P 289038-37-5P 289038-38-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 289038-39-7P 289038-40-0P 289038-41-1P 289038-42-2P 289038-43-3P
289038-44-4P 289038-45-5P 289056-45-7P 289056-46-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 1426-54-6P 1515-89-5P 3670-91-5P 5437-45-6P, Benzyl 2-bromoacetate 15886-84-7P 24632-01-7P 24765-57-9P 70132-87-5P 120454-34-4P 120936-00-7P 120936-01-8P 162632-54-4P 163445-43-0P 178678-21-2P 178678-55-2P 178678-56-3P 178678-60-9P 178678-61-0P 178678-62-1P 178678-64-3P 178678-67-6P 178678-68-7P 178678-72-3P 178678-73-4P 197373-46-9P 197378-07-7P 197378-13-5P 197378-15-7P 197378-16-8P 197378-18-0P 197378-20-4P 197378-22-6P 197378-24-8P 197378-26-0P 197378-29-3P 197378-31-7P 197378-32-8P 197378-34-0P 197378-36-2P 197378-38-4P 197378-40-8P 197378-42-0P 197378-44-2P 197378-46-4P 197378-48-6P 197378-50-0P 197378-52-2P 197378-54-4P 197378-56-6P 197378-58-8P 213312-71-1P 228113-57-3P 228113-58-4P 228113-59-5P 228113-61-9P 228113-62-0P 228113-63-1P 228113-64-2P 228113-65-3P 288863-77-4P 289038-46-6P 289038-47-7P 289038-48-8P 289038-49-9P 289038-50-2P 289038-51-3P 289038-52-4P 289038-53-5P 289038-54-6P 289038-55-7P 289038-56-8P 289038-57-9P 289038-58-0P 289038-59-1P 289038-60-4P 289038-61-5P 289038-62-6P 289038-63-7P 289038-64-8P 289038-65-9P 289038-66-0P 289038-67-1P 289038-68-2P 289038-69-3P 289038-70-6P 289038-72-8P 289038-74-0P 289038-75-1P 289038-77-3P 289038-78-4P 289038-79-5P 289038-80-8P 289038-81-9P 289038-82-0P 289038-83-1P 289038-84-2P 289038-86-4P 289038-87-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 56-41-7, L-Alanine, biological studies 57-88-5, Cholesterol, biological studies 81-24-3 9027-63-8, Cholesterol acyl transferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 197372-68-2P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 647859-02-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 197373-53-8P 280105-79-5P 280105-80-8P 280105-82-0P 280105-83-1P 280105-84-2P 280105-91-1P 280105-92-2P 280105-94-4P 280105-98-8P 280106-01-6P 280106-02-7P 280106-04-9P 280106-05-0P 280106-06-1P 280106-08-3P 280106-09-4P 280106-10-7P 280106-11-8P 280106-12-9P 289039-86-7P 289039-87-8P 289039-88-9P 289039-90-3P 289039-91-4P 289039-93-6P 289039-95-8P 289039-96-9P 289039-97-0P 289039-98-1P 289039-99-2P 289040-00-2P 289040-01-3P 647859-03-8P 647859-04-9P 647859-05-0P 647859-06-1P 647859-07-2P 647859-08-3P 647859-09-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 28994-41-4, 2-Hydroxydiphenylmethane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 51-45-6, Histamine, reactions 55-98-1, Busulfan 68-12-2, reactions 100-66-3, reactions 106-41-2, 4-Bromophenol 110-86-1, Pyridine, reactions 110-91-8, Morpholine, reactions 111-24-0, 1,5-Dibromopentane 111-96-6, 2-Methoxyethyl ether 123-12-6, N,N,N',N'-Tetraethyl diethylenetriamine 123-75-1, Pyrrolidine, reactions 131-57-7, 2-Hydroxy-4-methoxybenzophenone 138-60-3, Chelidamic acid 150-19-6, 3-Methoxyphenol 150-76-5, 4-Methoxyphenol 280-57-9, 1,4-Diazabicyclo[2.2.2]octane 352-11-4, 4-Fluorobenzyl chloride 371-41-5, 4-Fluorophenol 503-29-7, Azetidine 504-63-2, 1,3-Propanediol 596-75-8 623-25-6, α,α'-Dichloro-p-xylene 628-11-5, 3-Chloropropyl chloroformate 628-77-3, 1,5-Diiodopentane 696-63-9, 4-Methoxythiophenol 705-29-3, 3-(Trifluoromethyl)benzyl chloride 824-98-6, 3-Methoxybenzyl chloride 869-24-9, 2-Diethylaminoethyl chloride hydrochloride 922-63-4, 2-Ethylacrolein 1120-71-4, 1,3-Propane sultone 1633-83-6, 1,4-Butane sultone 1680-78-0, 2-Ethyl-2-(hydroxymethyl)hexanal 1801-99-6, 2-Mercaptobenzophenone 1822-51-1, 4-Picolyl chloride hydrochloride 2043-61-0, Cyclohexanecarboxaldehyde 2417-72-3, Methyl 4-(bromomethyl)benzoate 2516-96-3, 2-Chloro-5-nitrobenzoic acid 2646-90-4, 2,5-Difluorobenzaldehyde 3099-28-3, 2,6-Bis(chloromethyl)pyridine 4509-90-4, 5-Bromovaleroyl chloride 4521-31-7 4724-56-5 5414-19-7, Bis(2-bromoethyl)ether 5469-66-9, 1,3-Propanediol di-p-tosylate 6290-05-7 7136-51-8, N,N,N',N'-Tetraethyl 1,6-hexanediamine 13331-27-6, 3-Nitrobenzeneboronic acid 15014-25-2, Dibenzyl malonate 15852-73-0 34052-37-4, 2-Chloro-5-nitrobenzophenone 36839-55-1, 1,2-Bis(2-iodoethoxy)ethane 41602-50-0, N-(Chloroacetyl)glycine ethyl ester 60343-28-4, Benzyl 5-bromovalerate 63024-77-1, 3-Chloromethylbenzoyl chloride 121559-53-3 128114-91-0 175172-61-9 178678-63-2 178678-65-4 178678-66-5 197378-60-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

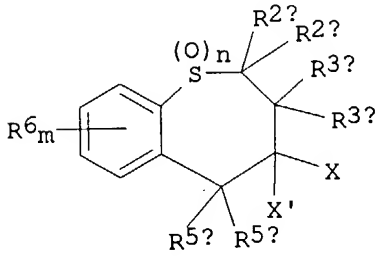
L19 ANSWER 3 OF 13 MARPAT COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	138:385315 MARPAT
TITLE:	Mono- and di-fluorinated benzothiepines as inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions and methods for preparation
INVENTOR(S):	Koeller, Kevin J.; Tremont, Samuel J.
PATENT ASSIGNEE(S):	G.D. Searle and Co., USA
SOURCE:	PCT Int. Appl., 589 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040127	A1	20030515	WO 2002-US35257	20021104
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004067872	A1	20040408	US 2002-286987	20021104
US 6740663	B2	20040525		
EP 1448546	A1	20040825	EP 2002-778711	20021104
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
PRIORITY APPLN. INFO.:			US 2001-330892P	20011102
			WO 2002-US35257	20021104

GI



I

AB Mono-fluorinated and di-fluorinated benzothiepine apical Na co-dependent bile acid transport (ASBT) inhibitors (shown as I; variables defined below; no specific examples are included) are disclosed together with methods of making the same, methods of using the same to treat hyperlipidemic conditions as well as pharmaceutical compns. containing the same compds. For I: X = F, X' = H, F; n = 0-2; m = 0-4; R2A and R2B = H and hydrocarbyl; R3A, R3B, R5A, and R5B = H, alkyl, cycloalkyl, alkenyl, alkynyl, heterocyclyl, quaternary heterocyclyl, oxo, aryl-R5, -OR9, -NR9R10, -SR9, -S(O)R9, -SO2R9, and -SO3R9; R9 and R10 = H, hydrocarbyl, amino, and hydrocarbylamino. R5 = H, hydrocarbyl, heterocyclyl, quaternary heterocyclyl, -OR9, -SR9, -S(O)R9, -SO2R9, and -SO3R9; ≥1 R6 radicals = H, halogen, -CN, -NO2, hydrocarbyl, -R5, -OR13, -NR 13R14, -SR13, -S(O)R13, -S(O)2R13, -SO3R13, -S+R3R14A-, -NR13OR14, -NR13NR14R15, -OM, -SO2OM, -SO2NR13R14, -NR14C(O)R13, -C(O)OM, -S(O)NR13R14, -N+R13R14R15A-, -PR13R14, -P(O)R13R4, -P+R13R14R15A-, amino acid residue, peptide residue, polypeptide residue, and carbohydrate residue; addnl. details are given in the claims. I (X = X' = F) are

claimed to be preparable from the 4-oxo analog and diethylaminosulfur trifluoride; I (X = F; X' = H) are claimed preparable from the 4-hydroxy analog and diethylaminosulfur trifluoride. Hundreds of example prepns. of precursors to I are included, but none of I; most of the example prepns. have appeared in earlier patents (e.g. WO 98/40375). Biol. testing procedures are described but no test results are reported except for the statement that a polyethylene glycol-functionalized benzothiepine (4500 MW; a 4-hydroxy analog of I) inhibited ileal bile acid transport-mediated uptake of 14C-taurocholate in H14 cells.

IC ICM C07D337-00
ICS A61K031-38

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST fluorinated benzothiepine prepn method inhibitor ASBT taurocholate uptake hyperlipidemic

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ASBT (apical sodium-dependent bile acid transporter), inhibitors; preparation of novel mono- and di-fluorinated benzothiepines as inhibitors
of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ASBT inhibitors; preparation of novel mono- and di-fluorinated benzothiepines as inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT Calculi, biliary
(dissolving agents; preparation of novel mono- and di-fluorinated benzothiepines as inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT Drug delivery systems
(for mono- and di-fluorinated benzothiepines as inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of novel mono- and di-fluorinated benzothiepines as inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT Anticholesteremic agents
Biological transport
Calculi, biliary
Human
Hypercholesterolemia
(preparation of novel mono- and di-fluorinated benzothiepines as inhibitors
of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 7440-23-5, Sodium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ASBT inhibitors; preparation of novel mono- and di-fluorinated benzothiepines as inhibitors of apical sodium co-dependent bile acid

transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 361373-74-2P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(formation and racemization; preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 197372-68-2P, 3-Butyl-3-ethyl-4,5-dihydroxy-5-phenyl-2,3,4,5-tetrahydrobenzothiepine-1,1-dioxide 197378-62-4P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 197373-36-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 228113-60-8P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 228113-65-3P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 51-45-6, Histamine, reactions 55-98-1, Busulfan 66-25-1, Hexanal 91-22-5, Quinoline, reactions 100-47-0, Benzonitrile, reactions 100-66-3, Anisole, reactions 106-41-2, 4-Bromophenol 106-44-5, 4-Methylphenol, reactions 108-98-5, Thiophenol, reactions 109-00-2, 3-Hydroxypyridine 109-89-7, Diethylamine, reactions 110-18-9, N,N,N',N'-Tetramethylethylenediamine 110-86-1, Pyridine, reactions 110-91-8, Morpholine, reactions 111-18-2, N,N,N',N'-Tetramethyl-1,6-hexanediamine 111-24-0, 1,5-Dibromopentane 121-44-8, Triethylamine, reactions 121-86-8, 2-Chloro-4-nitrophenylmethane 123-12-6, N,N,N',N'-Tetraethyldiethylenetriamine 123-75-1, Pyrrolidine, reactions 131-57-7, 2-Hydroxy-4-methoxybenzophenone 138-60-3, Chelidamic acid 150-76-5, 4-Methoxyphenol 280-57-9, 1,4-Diazabicyclo[2.2.2]octane 345-35-7, 2-Fluorobenzyl chloride 352-11-4, 4-Fluorobenzyl chloride 371-41-5, 4-Fluorophenol 456-42-8, 3-Fluorobenzyl chloride 462-06-6, Fluorobenzene 503-29-7, Azetidine 504-63-2, 1,3-Propanediol 596-75-8, Diethyl dibutylmalonate 623-25-6, α,α'-Dichloro-p-xylene 628-11-5, 3-Chloropropyl chloroformate 628-77-3, 1,5-Diiodopentane 696-63-9, 4-Methoxythiophenol 705-29-3, 3-(Trifluoromethyl)benzyl chloride 824-98-6, 3-Methoxybenzyl chloride 869-24-9, 2-Diethylaminoethyl chloride hydrochloride 922-63-4, 2-Ethylacrolein 1633-83-6, 1,4-Butane sultone 1642-81-5, 4-(Chloromethyl)benzoic acid 1680-78-0, 2-Ethyl-2-(hydroxymethyl)hexanal 1801-99-6, 2-Mercaptobenzophenone 1822-51-1, 4-Picolyl chloride

hydrochloride 2043-61-0, Cyclohexanecarboxaldehyde 2417-72-3, Methyl 4-(bromomethyl)benzoate 2516-96-3, 2-Chloro-5-nitrobenzoic acid 2646-90-4, 2,5-Difluorobenzaldehyde 3099-28-3, 2,6-Bis(chloromethyl)pyridine 4023-02-3, 1H-Pyrazole-1-carboxamidine hydrochloride 4509-90-4, 5-Bromovaleroyl chloride 4521-31-7, 2-Mercaptobenzyl alcohol 4724-56-5 5414-19-7, Bis(2-bromoethyl) ether 5437-45-6, Benzyl 2-bromoacetate 5469-66-9, 1,3-Propanediol di-p-tosylate 6290-05-7 9004-74-4, MPEG 13331-27-6, 3-Nitrobenzeneboronic acid 15014-25-2, Dibenzyl malonate 16420-13-6, Dimethylthiocarbamoyl chloride 18982-54-2, 2-Bromobenzyl alcohol 28994-41-4, 2-Hydroxydiphenylmethane 34052-37-4, 2-Chloro-5-nitrobenzophenone 35730-09-7, 2,5-Difluorobenzoyl chloride 36839-55-1, 1,2-Bis(2-iodoethoxy)ethane 41602-50-0, N-(Chloroacetyl)glycine ethyl ester 60343-28-4, Benzyl 5-bromovalerate 63024-77-1, 3-Chloromethylbenzoyl chloride 99376-14-4 121559-53-3 154932-88-4 197372-97-7 197372-98-8 197373-14-1 197375-48-7 197375-49-8 197378-59-9 197378-60-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 1426-54-6P, 4-Fluoro-2-[(4-methoxyphenyl)methyl]phenol 1481-12-5P, 4-Fluoro-2-(4'-fluorobenzyl)phenol 1515-89-5P, 3-Bromobenzyl methyl ether 3670-91-5P 15886-84-7P 16473-35-1P, 1-(Chloromethyl)-4-(hydroxymethyl)benzene 24632-01-7P, 1-(Hydroxymethyl)cyclohexanecarboxaldehyde 24765-57-9P, 2,2-Dibutyl-1,3-propanediol 70132-87-5P 120454-34-4P, 2-Mercaptodiphenylmethane 120936-00-7P, O-2-Benzylphenyl dimethylthiocarbamate 120936-01-8P 131117-88-9P 162632-54-4P, 2-Mercapto-4-methoxybenzophenone 163445-43-0P, 2-Mercapto-5-methoxybenzophenone 174747-95-6P, 1-Bromo-2-butyl-2-(hydroxymethyl)hexane 178678-21-2P 178678-22-3P, 3-Butyl-3-ethyl-5-phenyl-2,3-dihydrobenzothiepine 178678-23-4P, cis-3-Butyl-3-ethyl-5-phenyl-2,3-dihydrobenzothiepin-4(5H)-one 178678-24-5P, trans-3-Butyl-3-ethyl-5-phenyl-2,3-dihydrobenzothiepin-4(5H)-one 178678-25-6P, cis-3-Butyl-3-ethyl-5-phenyl-2,3-dihydrobenzothiepin-4(5H)-one-1,1-dioxide 178678-26-7P 178678-27-8P 178678-29-0P 178678-33-6P, 3-Ethyl-5-phenyl-2,3-dihydrobenzothiepine 178678-34-7P 178678-36-9P, cis-3-Ethyl-5-phenyl-2,3,4,5-tetrahydrobenzothiepine-1,1-dioxide 178678-37-0P 178678-40-5P 178678-45-0P 178678-46-1P 178678-49-4P 178678-50-7P 178678-51-8P 178678-55-2P 178678-56-3P, 2-[(2-Benzoylphenylthio)methyl]-2-ethylhexanal 178678-57-4P, 2-[(2-Benzoylphenylthio)methyl]butyraldehyde 178678-58-5P 178678-59-6P 178678-60-9P 178678-61-0P 178678-62-1P 178678-63-2P 178678-64-3P 178678-65-4P 178678-66-5P 178678-67-6P 178678-68-7P 178678-69-8P 178678-70-1P 178678-71-2P 178678-72-3P 178678-73-4P 178897-97-7P 178898-00-5P 178898-01-6P 178898-05-0P 197372-67-1P 197372-71-7P 197372-76-2P 197372-77-3P 197372-78-4P 197373-02-7P 197373-03-8P 197373-13-0P 197373-42-5P 197373-43-6P 197373-44-7P 197373-46-9P 197373-47-0P 197373-49-2P 197373-50-5P 197373-51-6P 197373-52-7P 197373-55-0P 197373-56-1P 197373-57-2P 197373-58-3P 197377-84-7P 197378-05-5P 197378-07-7P, 4-Chloro-3-(4-methoxyphenylmethyl)nitrobenzene 197378-15-7P 197378-16-8P 197378-18-0P 197378-20-4P 197378-22-6P 197378-24-8P 197378-26-0P 197378-29-3P 197378-31-7P 197378-32-8P 197378-34-0P 197378-36-2P 197378-38-4P 197378-40-8P 197378-42-0P 197378-44-2P 197378-46-4P 197378-48-6P, 4-Fluoro-2-(3'-methoxybenzyl)phenol 197378-50-0P 197378-52-2P

197378-54-4P 197378-56-6P 197378-58-8P 228113-57-3P 228113-58-4P
228113-59-5P 228113-63-1P 228113-64-2P 270931-13-0P 270931-14-1P
270931-15-2P 288863-77-4P 289037-96-3P 289037-98-5P 289038-46-6P
289038-47-7P 289038-49-9P 289038-51-3P 289038-52-4P 289038-53-5P
289038-54-6P 289038-55-7P 289038-56-8P 289038-57-9P 289038-58-0P
289038-59-1P 289038-60-4P 289038-61-5P 289038-63-7P 289038-64-8P
289038-65-9P 289038-66-0P 289038-68-2P 289038-69-3P 289038-70-6P
289038-72-8P 289038-74-0P 289038-75-1P 289038-77-3P 289038-78-4P
289038-79-5P 289038-80-8P 289038-81-9P 289038-82-0P 289038-83-1P
289038-84-2P 289038-86-4P 289038-87-5P 361373-66-2P,
2-(Bromomethyl)-2-butylhexanal 361374-22-3P 361374-31-4P,
3-Acetoxy-2,2-dibutyl-1-propanol 525589-60-0P 525589-61-1P
525589-62-2P 525589-63-3P 525589-64-4P 525589-65-5P,
4-Methyl-2-(4'-fluorobenzyl)phenol 525589-69-9P 525589-71-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 178678-28-9P, 3-Butyl-3-ethyl-5-phenyl-2,3-dihydrobenzothiepine-1,1-dioxide 178678-30-3P, cis-3-Butyl-3-ethyl-5-phenyl-2,3,4,5-tetrahydrobenzothiepine-1,1-dioxide 178678-31-4P, trans-3-Butyl-3-ethyl-5-phenyl-2,3,4,5-tetrahydrobenzothiepine-1,1-dioxide 178678-32-5P,
3-Butyl-3-ethyl-4-hydroxy-5-cyclohexylidene-2,3,4,5-tetrahydrobenzothiepine-1,1-dioxide 178678-35-8P 178678-38-1P
178678-39-2P 178678-41-6P 178678-44-9P 178678-47-2P 178678-48-3P
178678-52-9P 178678-53-0P 178678-54-1P 178897-95-5P 178897-96-6P
178897-99-9P 178898-02-7P 178898-03-8P 178898-04-9P 197372-66-0P
197372-70-6P 197372-72-8P 197372-73-9P 197372-74-0P 197372-75-1P
197372-79-5P 197372-80-8P 197372-81-9P 197372-82-0P 197372-83-1P
197372-84-2P 197372-85-3P 197372-86-4P 197372-87-5P 197372-88-6P
197372-90-0P 197373-06-1P 197373-16-3P 197373-17-4P 197373-18-5P
197373-19-6P 197373-20-9P 197373-22-1P 197373-24-3P 197373-25-4P
197373-26-5P 197373-27-6P 197373-32-3P 197373-35-6P 197373-38-9P
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197373-54-9P 197373-59-4P 197377-85-8P 197377-86-9P 197377-90-5P
197377-94-9P 197377-96-1P 197377-98-3P 197378-13-5P 228113-66-4P
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289037-61-2P 289037-62-3P 289037-64-5P 289037-65-6P 289037-67-8P
289037-68-9P 289037-70-3P 289037-72-5P 289037-74-7P 289037-75-8P
289037-76-9P 289037-77-0P 289037-78-1P 289037-79-2P 289037-80-5P
289037-81-6P 289037-82-7P 289037-83-8P 289037-84-9P 289037-85-0P
289037-86-1P 289037-87-2P 289037-88-3P 289037-90-7P 289037-91-8P
289037-92-9P 289037-93-0P 289037-94-1P 289037-97-4P 289037-99-6P
289038-50-2P 361374-26-7P 525589-59-7P 526199-85-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of precursors of mono- and di-fluorinated benzothiepine inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

IT 81-24-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(uptake inhibitors; preparation of novel mono- and di-fluorinated benzothiepines as inhibitors of apical sodium co-dependent bile acid transport (ASBT) and taurocholate uptake for treating hyperlipidemic conditions)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

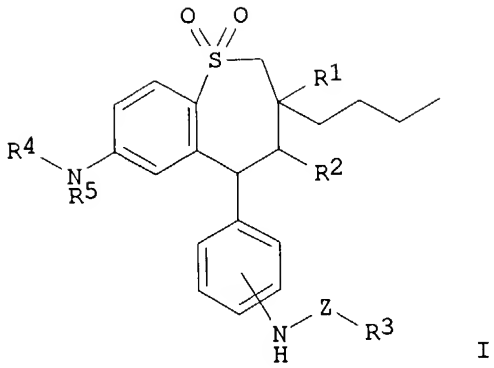
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:215326 MARPAT
TITLE: Combined preparations, containing 1,4-benzothiepine-1,1-dioxide derivatives and other active substances for the treatment of hyperlipidemia
INVENTOR(S): Glombik, Heiner; Frick, Wendelin; Schaefer, Hans-Ludwig; Kramer, Werner
PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018024	A1	20030306	WO 2002-EP8908	20020809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10140169	A1	20030306	DE 2001-10140169	20010822
DE 10142456	A1	20030320	DE 2001-10142456	20010831
EP 1425018	A1	20040609	EP 2002-796213	20020809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.:
DE 2001-10140169 20010822
DE 2001-10142456 20010831
WO 2002-EP8908 20020809

GI



I

AB The invention relates to mixts. of substances, containing 1,4-benzothiepine-1,1-dioxide derivs. of formula (I), in which the functional groups have the indicated meanings, their physiol. acceptable salts and physiol. functional derivs. as well as other active substances for the treatment of metabolic disorders especially hyperlipidemia. The combinations can also include antidiabetics, antiarthrytics etc. A typical capsule contains 100 mg of the drugs and 400 mg triglyceride mixture from coco fatty acids; other formulations are emulsions, tablets, dragees, and solns. Hamster that were fed with cholesterol-rich feed received orally the drug combination once daily for 10 days. Feces was analyzed for bile acids, blood lipid levels were measured and cholesterol was determined from liver.

IC ICM A61K031-55
ICS A61K031-395; A61P003-06

CC 1-10 (Pharmacology)
Section cross-reference(s): 63

ST benzothiepine dioxide combination drug anticholesterimics antilipemic agent

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ATP-sensitive, binding drugs; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CRF-binding protein, antagonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Lipoprotein receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL, inducers; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Lp(a), antagonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(MTP (microsomal triglyceride-exchanging protein), inhibitors; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RXR, modulators; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(a/γ, agonists; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(adsorbers; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonist; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Drug delivery systems
(capsules; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cholesterol ester-exchanging, inhibitors; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 5-HT agonists
Antiarthritics
Anticholesteremic agents
Antidiabetic agents
Antioxidants
Hypercholesterolemia
Hypolipemic agents
(combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Sulfonylureas
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Drug delivery systems
(dragees; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Drug delivery systems
(emulsions; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Neurotransmitter agonists
(histaminic H3, agonists; combined preps., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(hyperlipidemia; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 4, MT-4, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide, cocaine and amphetamine-regulated transcript peptide, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resorption inhibitors; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Drug delivery systems
(tablets; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Thyroid hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 9015-71-8, CRF 245359-74-4, Orexin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonist; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 9002-79-3, Melanocyte-stimulating hormone 9011-97-6, Cholecystokinin 24305-27-9, TRH 31362-50-2, Bombesin 82785-45-3, Neuropeptide Y 193830-48-7, Urocortin 202347-31-7, Leptin E
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 119418-04-1, Galanin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 57-88-5, Cholesterol, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 56-03-1, Biguanide 300-62-9, Amphetamine 943-45-3, Fibric acid 2295-31-0, Glitazone 5395-30-2 9000-40-2, Carob gum 9002-72-6, Growth hormone 9004-10-8, Insulin, biological studies 9034-39-3, Growth hormone releasing hormone 11041-12-6, Cholestyramine 25614-03-3, Bromocriptine 25812-30-0, Gemfibrozil 49642-07-1, Statine 50925-79-6, Cholestipol 54870-28-9, Meglitinide 96829-58-2, Orlistat 99759-19-0, Tiqueside 129024-87-9, Doprexin 150332-35-7, Pamaqueside 163222-33-1, Ezetimibe 252047-40-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 9000-92-4, Amylase 9027-63-8, ACAT
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 50-67-9, biological studies 9001-42-7, α-Glucosidase 9001-62-1, Lipase 9004-02-8, Lipoprotein-Lipase 9027-95-6, ATP-Citrate-Lyase 9028-35-7, HMG-CoA-Reductase 9077-14-9, Squalene synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:215324 MARPAT
TITLE: Combined preparations, containing 1,4-benzothiepine-1,1-dioxide derivatives and other active substances for the treatment of hyperlipidemia
INVENTOR(S): Glombik, Heiner; Frick, Wendelin; Schaefer, Hans-Ludwig; Kramer, Werner
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10140169	A1	20030306	DE 2001-10140169	20010822
WO 2003018024	A1	20030306	WO 2002-EP8908	20020809

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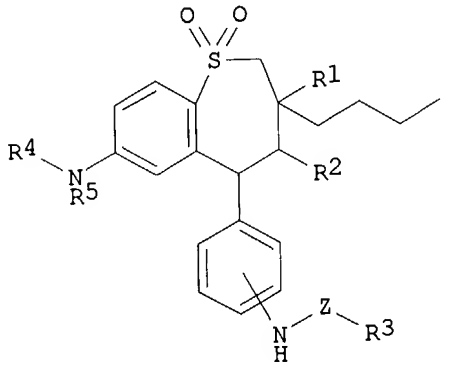
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,

NE, SN, TD, TG
EP 1425018 A1 20040609 EP 2002-796213 20020809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
US 2003158119 A1 20030821 US 2002-225841 20020822
US 2004097424 A1 20040520 US 2003-699967 20031103
PRIORITY APPLN. INFO.: DE 2001-10140169 20010822
DE 2001-10142456 20010831
WO 2002-EP8908 20020809
US 2002-225841 20020822

GI



I

AB The invention relates to mixts. of substances, containing 1,4-benzothiepine-1,1-dioxide derivs. of formula (I), in which the functional groups have the indicated meanings, their physiol. acceptable salts and physiol. functional derivs. as well as other active substances for the treatment of metabolic disorders especially hyperlipidemia. The combination can also include antidiabetics, antiarthrytics etc. A typical capsule contains 100 mg of the drugs and 400 mg triglyceride mixture form coco fatty acids; other formulations are emulsions, tablets, dragees, and solns. The inhibition of sodium-dependent uptake of [3H]-taurocholate (TC) into brush border membrane vesicles was measured.

IC ICM A61K038-07
ICS A61K038-06; A61K038-05; A61K031-7008
CC 1-10 (Pharmacology)
Section cross-reference(s): 63
ST benzothiepine dioxide combination drug anticholesterimics antilipemic agent
IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ATP-sensitive, binding drugs; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CRF-binding protein, antagonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Lipoprotein receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL, inducers; combined prepns., containing
1,4-benzothiepine-1,1-dioxide
derivs. and other active substances for treatment of hyperlipidemia)

IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Lp(a), antagonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MTP (microsomal triglyceride-exchanging protein), inhibitors; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other
active
substances for treatment of hyperlipidemia)

IT Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RXR, modulators; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(a/γ agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonist; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Drug delivery systems
(capsules; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cholesterol ester-exchanging, inhibitors; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 5-HT agonists
Antiarthritics
Anticholesteremic agents
Antidiabetic agents
Antioxidants
Hypercholesterolemia
Hypolipemic agents
(combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Sulfonylureas
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Drug delivery systems
(dragees; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Drug delivery systems

(emulsions; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Neurotransmitter agonists
(histaminic H3, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 4, MT-4, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide, cocaine and amphetamine-regulated transcript peptide, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polymeric, adsorbers; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resorption inhibitors; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sodium dependent taurocholate, inhibition of; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Drug delivery systems
(tablets; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Thyroid hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 9015-71-8, CRF 245359-74-4, Orexin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonist; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 9002-79-3, Melanocyte-stimulating hormone 9011-97-6, Cholecystokinin
24305-27-9, TRH 31362-50-2, Bombesin 82785-45-3, Neuropeptide Y
169494-85-3, Leptin 193830-48-7, Urocortin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 119418-04-1, Galanin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 56-03-1, Biguanide 300-62-9, Amphetamine 943-45-3, Fibric acid
2295-31-0, 2,4-Thiazolidinedione 5395-30-2 9002-72-6, Growth hormone
9004-10-8, Insulin, biological studies 9034-39-3, Growth hormone releasing hormone 11041-12-6, Cholestyramine 25614-03-3, Bromocriptine
25812-30-0, Gemfibrozil 49642-07-1, Statine 50925-79-6, Cholestipol
54870-28-9, Meglitinide 96829-58-2, Orlistat 99759-19-0, Tiqueside
129024-87-9, Doprexin 150332-35-7, Pamaqueside 163222-33-1, Ezetimibe
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 9000-92-4, Amylase 9027-63-8, ACAT
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 50-67-9, biological studies 9001-42-7, α-Glucosidase 9001-62-1, Lipase 9004-02-8, Lipoprotein-Lipase 9027-95-6, ATP-Citrate-Lyase
9028-35-7, HMG-CoA-Reductase 9077-14-9, Squalene synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

IT 81-24-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sodium dependent uptake, inhibition of; combined prepns., containing 1,4-benzothiepine-1,1-dioxide derivs. and other active substances for treatment of hyperlipidemia)

L19 ANSWER 6 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 137:63115 MARPAT
TITLE: Preparation of diphenylazetidinone derivatives as hypolipidemic agents
INVENTOR(S): Glombik, Heiner; Kramer, Werner; Flohr, Stefanie; Frick, Wendelin; Heuer, Hubert; Jaehne, Gerhard;

PATENT ASSIGNEE(S): Lindenschmidt, Andreas; Schaefer, Hans-Ludwig
Aventis Pharma Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050068	A1	20020627	WO 2001-EP14532	20011211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10064402	A1	20020627	DE 2000-10064402	20001221
DE 10154520	A1	20031002	DE 2001-10154520	20011107
AU 2002019173	A5	20020701	AU 2002-19173	20011211
EE 200300237	A	20030815	EE 2003-237	20011211
EP 1345932	A1	20030924	EP 2001-271371	20011211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001016482	A	20040203	BR 2001-16482	20011211
JP 2004516293	T2	20040603	JP 2002-551564	20011211
US 2002128252	A1	20020912	US 2001-21028	20011219
US 6498156	B2	20021224		
NO 2003002733	A	20030814	NO 2003-2733	20030616

PRIORITY APPLN. INFO.: DE 2000-10064402 20001221
DE 2001-10154520 20011107
WO 2001-EP14532 20011211

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The compds. are suited for use e.g. as hypolipidemic drugs. The invention discloses preparation of diphenylazetidinone derivs. such as I [R1, R2, R3, R4,

R5, R6 = C0-C30-alkylene-L {optionally containing O, CO, CH:CH, C.tplbond.C, N(alkyl), N(alkylphenyl), NH}, H, F, Cl, Br, I, CF3, NO2, CN, CO2H, CO2(alkyl), CONH2, CONH(alkyl), CON(alkyl)2, alkyl, alkenyl, alkynyl, O-alkyl, SO2NH2, SO2NH(alkyl) SO2N(alkyl)2, S-(alkyl), SO(alkyl), (un)substituted S(CH2)nPh, SO(CH2)nPh, SO2(alkyl), SO2(CH2)nPh, NH2, NH(alkyl), N(alkyl)2, NH(acyl), (un)substituted Ph, O(CH2)nPh; n = 0-6; L = II; R7, R9, R10 = Me, Et, Pr, butyl; R8 = H, OH, NH2, NH(alkyl)], and their physiol. acceptable salts, for their use as hypolipidemic agents. Thus, 1,2-diphenylazetidinone derivative III·trifluoroacetate (IV) was prepared via a multistep synthetic sequence starting from

7-[3-(3-butyl-7-dimethylamino-3-ethyl-4-hydroxy-1,1-dioxo-2,3,4,5-tetrahydro-1H-benzo[b]thiepin-5-yl)-phenylcarbamoyl]-heptanoic acid and 4-(4-aminomethylphenyl)-1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxyphenyl]-azetidin-2-one. Azetidinone IV was tested for its cholesterol lowering ability [ED50 = 0.01 mg/mouse].

IC ICM C07D409-12
ICS A61K031-397; A61P009-00

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63

ST azetidinone diphenyl deriv prepn hypolipidemic; diphenylazetidinone prepn hypolipidemic

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of diphenylazetidinone derivs. as hypolipidemics)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia, medicaments; preparation of diphenylazetidinone derivs. as hypolipidemics)

IT Diabetes mellitus
(insulin-resistant, medicaments; preparation of diphenylazetidinone derivs. as hypolipidemics)

IT Arteriosclerosis
(medicaments; preparation of diphenylazetidinone derivs. as hypolipidemics)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic disorders, medicaments; preparation of diphenylazetidinone derivs. as hypolipidemics)

IT Anticholesteremic agents
Antidiabetic agents
Human
Hypolipemic agents
(preparation of diphenylazetidinone derivs. as hypolipidemics)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, agonist; preparation of diphenylazetidinone derivs. as hypolipidemics)

IT 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments; preparation of diphenylazetidinone derivs. as hypolipidemics)

IT 439113-82-3P 439113-89-0P 439113-91-4P 439113-92-5P 439113-93-6P
439113-96-9P 439113-98-1P 439114-01-9P 439114-03-1P 439114-06-4P
439114-08-6P 439114-11-1P 439114-16-6P 439114-20-2P 439114-22-4P
439114-23-5P 439114-26-8P 439114-29-1P 439114-36-0P 439114-38-2P
439114-39-3P 439114-40-6P 439120-25-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diphenylazetidinone derivs. as hypolipidemics)

IT 76-05-1, Trifluoroacetic acid, reactions 112-60-7, Tetraethylene glycol 124-04-9, Hexanedioic acid, reactions 1117-97-1, O,N-Dimethylhydroxylamine 1501-05-9 1663-39-4, tert-Butyl acrylate 7480-32-2, 4-Phenyl-oxazolidin-2-one 20256-89-7 23243-68-7

402820-38-6 439080-96-3 439114-09-7 439114-17-7 439114-41-7
439114-42-8 439114-43-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diphenylazetidinone derivs. as hypolipidemics)

IT 94376-75-7P 439080-20-3P 439080-21-4P 439080-24-7P 439080-59-8P
439080-60-1P 439080-61-2P 439080-62-3P 439113-83-4P 439113-84-5P
439113-85-6P 439113-86-7P 439113-87-8P 439113-88-9P 439113-90-3P
439113-94-7P 439113-99-2P 439114-04-2P 439114-12-2P 439114-13-3P
439114-14-4P 439114-18-8P 439114-24-6P 439114-27-9P 439114-30-4P
439114-31-5P 439114-32-6P 439114-34-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diphenylazetidinone derivs. as hypolipidemics)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:257255 MARPAT
TITLE: preparation of chiral azaazoniabicyclooctylmethylbenzyloxyphenyltetrahydrobenzothiepines by amination of the corresponding benzyl alcohols.
INVENTOR(S): Babiak, Kevin A.; Carpenter, Andrew; Chou, Shine; Colson, Pierre-Jean; Farid, Payman; Hett, Robert; Huber, Chrisistian H.; Koeller, Kevin J.; Lawson, Jon P.; Li, James; Mar, Eduardo K.; Miller, Lawrence M.; Orlovski, Vladislav; Peterson, James C.; Pozzo, Mark J.; Przybyla, Claire A.; Tremont, Samuel J.; Trivedi, Jay S.; Wagner, Grace M.; Weisenburger, Gerald A.; Zhi, Benxin
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 258 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068637	A2	20010920	WO 2001-US7421	20010308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001040115	A5	20010924	AU 2001-40115	20010308
US 2002032329	A1	20020314	US 2001-802279	20010308
US 6586434	B2	20030701		
EP 1286984	A2	20030305	EP 2001-914762	20010308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003528830	T2	20030930	JP 2001-567729	20010308

US 2003236406	A1	20031225	US 2002-204826	20021223
US 2004082647	A1	20040429	US 2003-419266	20030421
US 2004110761	A1	20040610	US 2003-611942	20030703
PRIORITY APPLN. INFO.:			US 2000-188361P	20000310
			US 2000-188378P	20000310
			US 2001-802279	20010308
			US 2001-802313	20010308
			WO 2001-US7421	20010308

OTHER SOURCE(S): CASREACT 135:257255

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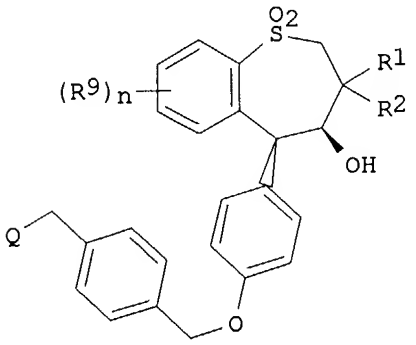

I

AB Title compds. [I; Q = (X-)R3R4R5N; R1, R2 = hydrocarbyl; R3-R5 = H, (O-, S-, or N-interrupted) hydrocarbyl; ≥2 of R3-R5 form a cyclic structure; R9 = H, hydrocarbyl, hydroxyalkyl, OR3, NR3R4, N+R3R4R5 A-, etc.; A- = pharmaceutically acceptable cation; X- = leaving group; n = 0-4], were prepared by derivatization of I (Q = OH; other variables as above) to give I (Q = X; other variables as above) and treatment of the latter with NR3R4R5. Thus, (4R,5R)-3,3-dibutyl-7-dimethylamino-1,1-dioxido-4-hydroxy-5-(4-hydroxyphenyl)-2,3,4,5-tetrahydrobenzothiepine (preparation given) in dimethylacetamide was treated with NaOH and then with 1-chloromethyl-4-hydroxymethylbenzene (preparation given) followed by heating at 50° for 4 h. The crude product was stirred with SOCl2 in PhMe and the chloromethyl product solution was treated with MeCOEt, H2O, and diazabicyclo[2.2.2]octane followed by reflux to give (4R,5R)-1-[[4-[4-(3,3-dibutyl-7-dimethylamino-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1-benzothiepin-5-yl)phenoxy]methyl]phenyl]methyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride.

IC ICM C07D337-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 45

ST azaazoniabicyclooctylmethylbenzyloxyphenyltetrahydrobenzothiepine prepn; benzothiepine dioxide dimethylamino tetrahydro azaazoniabicyclooctylmethylbenzyloxyphenyl prepn; hydroxymethylbenzyloxyphenyltetrahydrobenzothiepine amination DABCO

IT Amination
(preparation of chiral azaazoniabicyclooctylmethylbenzyloxyphenyltetrahydrobenzothiepines by amination of the corresponding benzyl alcs.)

IT 228113-66-4P 228113-67-5P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of chiral azaazoniabicyclooctylmethylbenzyloxyphenyltetrahydrob enzothiepines by amination of the corresponding benzyl alcs.)

IT 228113-64-2P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral azaazoniabicyclooctylmethylbenzyloxyphenyltetrahydrob enzothiepines by amination of the corresponding benzyl alcs.)

IT 100-66-3, Anisole, reactions 122-51-0, Triethylorthoformate 280-57-9, Dabco 507-09-5, Thiolacetic acid, reactions 596-75-8, Diethyl dibutylmalonate 598-32-3, 2-Hydroxy-3-butene 616-25-1, 1-Penten-3-ol 657-84-1 1070-66-2, 2-Butylacrolein 1642-81-5, 4-Chloromethylbenzoic acid 2463-63-0, Butylacrolein 2516-96-3, 2-Chloro-5-nitrobenzoic acid 5138-90-9, Benzenesulfonic acid, 4-chloro-, sodium salt 10387-40-3, Potassium thioacetate 56102-14-8 361374-10-9 361374-12-1 361374-17-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of chiral azaazoniabicyclooctylmethylbenzyloxyphenyltetrahydrob enzothiepines by amination of the corresponding benzyl alcs.)

IT 16473-35-1P 24765-57-9P 25784-91-2P 70132-87-5P 87897-57-2P 174747-95-6P 197373-42-5P 197378-07-7P 197378-31-7P 197378-32-8P 228113-65-3P 289038-78-4P 361373-66-2P 361373-74-2P 361373-79-7P 361373-81-1P 361373-83-3P 361373-85-5P 361373-87-7P 361373-89-9P 361373-91-3P 361373-92-4P 361373-94-6P 361373-96-8P 361373-98-0P 361374-00-7P 361374-02-9P 361374-04-1P 361374-06-3P 361374-08-5P 361374-16-5P 361374-18-7P 361374-19-8P 361374-20-1P 361374-22-3P 361374-24-5P 361374-26-7P 361374-28-9P 361374-31-4P 361374-33-6P 361374-36-9P 361374-39-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral azaazoniabicyclooctylmethylbenzyloxyphenyltetrahydrob enzothiepines by amination of the corresponding benzyl alcs.)

L19 ANSWER 8 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:193089 MARPAT
TITLE: Preparation of substituted 5-aryl-benzothiepines as ileal bile acid transport and taurocholate uptake inhibitors
INVENTOR(S): Lee, Len F.; Banerjee, Shyamal C.; Huang, Horng-chih; Li, Jinglin J.; Miller, Raymond E.; Reitz, David B.; Tremont, Samuel J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 191 pp., Cont.-in-part of U. S. Ser. No. 109,551.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6107494	A	20000822	US 1999-275463	19990324
EP 1440972	A1	20040728	EP 2004-10088	19970311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
US 5994391	A	19991130	US 1998-109551	19980702
EP 1331225	A1	20030730	EP 2003-5459	19981216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CA 2336315	AA	20000113	CA 1999-2336315	19990629
WO 2000001687	A1	20000113	WO 1999-US12828	19990629
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9948202	A1	20000124	AU 1999-48202	19990629
AU 766957	B2	20031030		
EP 1091953	A1	20010418	EP 1999-931769	19990629
EP 1091953	B1	20031210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100824	T2	20010723	TR 2001-20010082	19990629
BR 9911737	A	20011211	BR 1999-11737	19990629
EE 200100002	A	20020617	EE 2001-2	19990629
JP 2002519418	T2	20020702	JP 2000-558091	19990629
NZ 509621	A	20030829	NZ 1999-509621	19990629
AT 256122	E	20031215	AT 1999-931769	19990629
US 6262277	B1	20010717	US 1999-443403	19991119
AU 761249	B2	20030529	AU 2000-53394	20000816
NO 2001000016	A	20010302	NO 2001-16	20010102
ZA 2001000028	A	20010725	ZA 2001-28	20010102
HR 2001000004	A1	20011231	HR 2001-4	20010102
BG 105206	A	20010928	BG 2001-105206	20010131
US 2002013476	A1	20020131	US 2001-828968	20010409
US 6387924	B2	20020514		
US 2002188119	A1	20021212	US 2002-72600	20020211
US 2003171426	A1	20030911	US 2002-76091	20020215
US 6642268	B2	20031104		
JP 2004203891	A2	20040722	JP 2004-50473	20040225
PRIORITY APPLN. INFO.:			US 1994-305526	19940913
			US 1995-517051	19950821
			US 1996-13119P	19960311
			US 1997-816065	19970311
			US 1997-831284	19970331
			US 1997-68170P	19971219
			US 1998-109551	19980702
			AU 1997-23266	19970311
			EP 1997-915976	19970311
			US 1997-40660P	19970311
			EP 1998-962044	19981216
			US 1999-275463	19990324
			JP 2000-558091	19990629
			WO 1999-US12828	19990629

Searcher : Shears 571-272-2528

US 1999-443403 19991119
US 2000-676466 20000929
US 2000-581897 20001002

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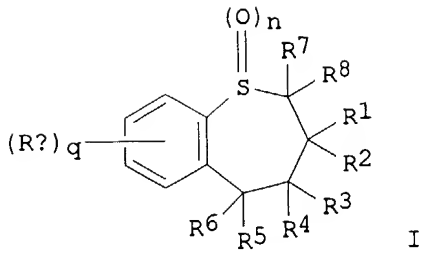

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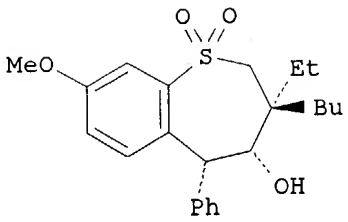

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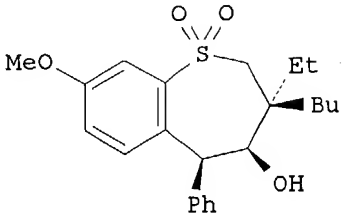

III

AB The title compds. (I) [wherein q = 1-4; n = 2; R1 and R2 = independently H or (un)substituted (halo)alkyl, alkenyl, alkynyl, alkylaryl, arylalkyl, alkoxy(alkyl), dialkylamino, alkylthio, (polyalkyl)aryl, or cycloalkyl; or R1 and R2 taken together with the atoms to which they are attached = cycloalkyl; R3 and R4 = independently H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocyclyl, OR9, NR9R10, SR9, S(O)R9, SO2R9, or SO3R9; R9 and R10 = independently H, (cyclo)alkyl, alkenyl, alkynyl, aryl(alkyl), acyl, heterocyclyl, or ammoniumalkyl; or R3 and R4 together = :O, :NOR11, :S, :NNR11R12, :NR9, or :CR11R12; R11 and R12 = independently H, (cyclo)alkyl, alkenyl, alkynyl, aryl(alkyl), heterocyclyl, carboxylalkyl, carboalkoxyalkyl, cyanoalkyl, OR9, NR9R10, SR9, S(O)R9, SO2R9, SO3R9, CO2R9, CN, halo, oxo, or CONR9R10; R5 = substituted aryl; R6 = H; R7 and R8 = independently H or alkyl; Rx = independently H or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, polyalkyl, acyloxy, aryl(alkyl), halo(alkyl), (quaternary) heterocyclyl, (quaternary) heteroaryl, polyether, alkoxy, amino, alkylthio, NO2, carboxy, carbamido, etc.] where prepared for the prophylaxis and treatment of hyperlipidemic conditions, such as those associated with atherosclerosis or hypercholesterolemia.

Thus, KOBu-t was added to a solution of 2-((2-benzyl-5-methoxyphenylsulfonyl)methyl)-2-ethylhexanal (preparation given) and dry THF cooled to -1.6°C to give, after workup, II and III (96% combined yield). The isomers were separated upon recrystn. II inhibited IBAT-mediated uptake of [14C]-taurocholate in H14 cells with an IC50 of 0.1 μM and reduced serum cholesterol from 143 mg (7%) to 126 mg (2%) compared to control in cholesterol-fed hamsters in a 14-day test. In vitro taurocholate uptake assay data are included for nearly 600 compds. of the invention.

Searcher : Shears 571-272-2528

IC C07D337-00; C07D487-00; A61K031-38; A61K031-495
NCL 549009000
CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
ST arylbenzothiepine prepn ileal bile acid transport inhibitor; benzothiepine prepn taurocholate uptake inhibitor; hypolipidemic antiatherosclerotic hypocholesterolemic arylbenzothiepine prepn
IT Antiarteriosclerotics
(antiatherosclerotics; preparation of substituted 5-aryl-benzothiepines by
cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)
IT Bile acids
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibition of ileal; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)
IT Anticholesteremic agents
Hypolipemic agents
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)
IT 178678-22-3P 178678-23-4P 178678-24-5P 178678-25-6P 178678-26-7P
178678-27-8P 178678-29-0P 178678-33-6P 178678-34-7P 178678-37-0P
178678-46-1P 178678-49-4P 178678-50-7P 178678-51-8P 178678-57-4P
178678-58-5P 178678-59-6P 178897-97-7P 178897-98-8P 178898-00-5P
178898-05-0P 197372-67-1P 197372-71-7P 197372-76-2P 197372-77-3P
197372-78-4P 197373-42-5P 197373-43-6P 197373-44-7P 197373-47-0P
197373-49-2P 197373-50-5P 197373-51-6P 197373-55-0P 197373-56-1P
197373-57-2P 197373-58-3P 197375-48-7P 197375-49-8P 289037-96-3P
289037-98-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)
IT 178678-28-9P 178678-30-3P 178678-31-4P 178678-35-8P 178678-36-9P
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178678-44-9P 178678-45-0P 178678-47-2P 178678-48-3P 178678-52-9P
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197373-03-8P 197373-04-9P 197373-05-0P 197373-06-1P 197373-07-2P
197373-08-3P 197373-09-4P 197373-10-7P 197373-11-8P 197373-12-9P
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197373-40-3P 197373-41-4P 197373-45-8P 197373-48-1P 197373-54-9P
197373-59-4P 197373-60-7P 197373-61-8P 197373-62-9P 197373-63-0P
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197373-70-9P 197373-71-0P 197373-72-1P 197373-73-2P 197373-75-4P
197373-76-5P 197373-77-6P 197373-78-7P 197373-79-8P 197373-80-1P
197373-81-2P 197373-83-4P 197373-85-6P 197373-87-8P 197373-90-3P
197373-93-6P 197373-95-8P 197373-97-0P 197373-99-2P 197374-00-8P
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197374-08-6P 197374-09-7P 197374-10-0P 197374-11-1P 197374-13-3P
197374-14-4P 197374-16-6P 197374-17-7P 197374-18-8P 197374-19-9P
197374-20-2P 197374-21-3P 197374-22-4P 197374-24-6P 197374-25-7P
197374-26-8P 197374-27-9P 197374-29-1P 197374-30-4P 197374-31-5P
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197374-39-3P 197374-40-6P 197374-41-7P 197374-43-9P 197374-44-0P
197374-45-1P 197374-46-2P 197374-47-3P 197374-48-4P 197374-49-5P
197374-50-8P 197374-51-9P 197374-52-0P 197374-53-1P 197374-54-2P
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197375-25-0P 197375-26-1P 197375-28-3P 197375-30-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 197375-32-9P 197375-34-1P 197375-39-6P 197375-42-1P 197375-44-3P
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197376-02-6P 197376-04-8P 197376-06-0P 197376-07-1P 197376-08-2P
197376-09-3P 197376-10-6P 197376-11-7P 197376-12-8P 197376-13-9P
197376-14-0P 197376-15-1P 197376-17-3P 197376-18-4P 197376-19-5P
197376-21-9P 197376-22-0P 197376-25-3P 197376-31-1P 197376-32-2P
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289037-55-4P 289037-56-5P 289037-57-6P 289037-58-7P 289037-59-8P
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289037-67-8P 289037-68-9P 289037-70-3P 289037-72-5P 289037-74-7P
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289038-30-8P 289038-32-0P 289038-33-1P 289038-34-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 289038-35-3P 289038-36-4P 289038-37-5P 289038-38-6P 289038-39-7P
289038-40-0P 289038-41-1P 289038-42-2P 289038-43-3P 289038-44-4P
289038-45-5P 289056-45-7P 289056-46-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hypolipemic agent; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 1426-54-6P 1515-89-5P 3670-91-5P 5437-45-6P, Benzyl 2-bromoacetate
15886-84-7P 24632-01-7P 24765-57-9P 70132-87-5P 120454-34-4P
120936-00-7P 120936-01-8P 162632-54-4P 163445-43-0P 178678-21-2P
178678-55-2P 178678-56-3P 178678-60-9P 178678-61-0P 178678-62-1P
178678-64-3P 178678-67-6P 178678-68-7P 178678-72-3P 178678-73-4P
197373-46-9P 197378-07-7P 197378-13-5P 197378-15-7P 197378-16-8P
197378-18-0P 197378-20-4P 197378-22-6P 197378-24-8P 197378-26-0P
197378-29-3P 197378-31-7P 197378-32-8P 197378-34-0P 197378-36-2P
197378-38-4P 197378-40-8P 197378-42-0P 197378-44-2P 197378-46-4P
197378-48-6P 197378-50-0P 197378-52-2P 197378-54-4P 197378-56-6P
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228113-61-9P 228113-62-0P 228113-63-1P 228113-64-2P 228113-65-3P
288863-77-4P 289038-46-6P 289038-47-7P 289038-48-8P 289038-49-9P
289038-50-2P 289038-51-3P 289038-52-4P 289038-53-5P 289038-54-6P

289038-55-7P 289038-56-8P 289038-57-9P 289038-58-0P 289038-59-1P
289038-60-4P 289038-61-5P 289038-62-6P 289038-63-7P 289038-64-8P
289038-65-9P 289038-66-0P 289038-67-1P 289038-68-2P 289038-69-3P
289038-70-6P 289038-72-8P 289038-74-0P 289038-75-1P 289038-77-3P
289038-78-4P 289038-79-5P 289038-80-8P 289038-81-9P 289038-82-0P
289038-83-1P 289038-84-2P 289038-86-4P 289038-87-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 289039-86-7P 289039-87-8P 289039-88-9P 289039-90-3P 289039-91-4P
289039-93-6P 289039-95-8P 289039-96-9P 289039-97-0P 289039-98-1P
289039-99-2P 289040-00-2P 289040-01-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 56-41-7, L-Alanine, biological studies 57-88-5, Cholesterol, biological studies 81-24-3 9027-63-8, Cholesterol acyl transferase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 197372-68-2P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 28994-41-4, 2-Hydroxydiphenylmethane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)

IT 51-45-6, Histamine, reactions 55-98-1, Busulfan 68-12-2, reactions 100-66-3, reactions 106-41-2, 4-Bromophenol 110-86-1, Pyridine, reactions 110-91-8, Morpholine, reactions 111-24-0, 1,5-Dibromopentane 111-96-6, 2-Methoxyethyl ether 123-12-6, N,N,N',N'-Tetraethyl diethylenetriamine 123-75-1, Pyrrolidine, reactions 131-57-7, 2-Hydroxy-4-methoxybenzophenone 138-60-3, Chelidamic acid 150-19-6, 3-Methoxyphenol 150-76-5, 4-Methoxyphenol 280-57-9, 1,4-Diazabicyclo[2.2.2]octane 352-11-4, 4-Fluorobenzyl chloride 371-41-5, 4-Fluorophenol 503-29-7, Azetidine 504-63-2, 1,3-Propanediol 596-75-8 623-25-6, α,α'-Dichloro-p-xylene 628-11-5, 3-Chloropropyl chloroformate 628-77-3, 1,5-Diiodopentane 696-63-9, 4-Methoxythiophenol 705-29-3, 3-(Trifluoromethyl)benzyl chloride 824-98-6, 3-Methoxybenzyl chloride 869-24-9, 2-Diethylaminoethyl chloride hydrochloride 922-63-4, 2-Ethylacrolein 1120-71-4, 1,3-Propane sultone 1633-83-6, 1,4-Butane sultone 1680-78-0, 2-Ethyl-2-(hydroxymethyl)hexanal 1801-99-6, 2-Mercaptobenzophenone 1822-51-1, 4-Picolyl chloride hydrochloride 2043-61-0, Cyclohexanecarboxaldehyde 2417-72-3, Methyl 4-(bromomethyl)benzoate 2516-96-3, 2-Chloro-5-nitrobenzoic acid 2646-90-4, 2,5-

Difluorobenzaldehyde 3099-28-3, 2,6-Bis(chloromethyl)pyridine 4509-90-4, 5-Bromovaleroyl chloride 4521-31-7 4724-56-5 5414-19-7, Bis(2-bromoethyl)ether 5469-66-9, 1,3-Propanediol di-p-tosylate 6290-05-7 7136-51-8, N,N,N',N'-Tetraethyl 1,6-hexanediamine 13331-27-6, 3-Nitrobenzeneboronic acid 15014-25-2, Dibenzyl malonate 15852-73-0 34052-37-4, 2-Chloro-5-nitrobenzophenone 36839-55-1, 1,2-Bis(2-iodoethoxy)ethane 41602-50-0, N-(Chloroacetyl)glycine ethyl ester 60343-28-4, Benzyl 5-bromovalerate 63024-77-1, 3-Chloromethylbenzoyl chloride 121559-53-3 128114-91-0 175172-61-9 178678-63-2 178678-65-4 178678-66-5 197378-60-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted 5-aryl-benzothiepines by cyclization of 2-((2-benzyl- and 2-benzoylphenylthio)methyl)alkanals as ileal bile acid transport and taurocholate uptake inhibitors)
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 132:35625 MARPAT
TITLE: Amino acid containing benzo[b]thiepine 1,1-dioxide derivatives as hypolipemic agents
INVENTOR(S): Frick, Wendelin; Enhsen, Alfons; Glombik, Heiner; Heuer, Hubert
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964410	A1	19991216	WO 1999-EP3701	19990528
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19825804	A1	19991216	DE 1998-19825804	19980610
DE 19825804	C2	20000824		
CA 2334775	AA	19991216	CA 1999-2334775	19990528
AU 9945019	A1	19991230	AU 1999-45019	19990528
AU 753275	B2	20021010		
EP 1086092	A1	20010328	EP 1999-927784	19990528
EP 1086092	B1	20021113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9912188	A	20010410	BR 1999-12188	19990528
TR 200003634	T2	20010621	TR 2000-20000363419990528	
JP 2002517491	T2	20020618	JP 2000-553419	19990528
AT 227715	E	20021115	AT 1999-927784	19990528
ES 2182535	T3	20030301	ES 1999-927784	19990528

PT 1086092	T	20030331	PT 1999-927784	19990528
RU 2215001	C2	20031027	RU 2001-101491	19990528
TR 200003632	T2	20010420	TR 2000-20000363	19990529
AU 761249	B2	20030529	AU 2000-53394	20000816
ZA 2000007060	A	20010718	ZA 2000-7060	20001130
ZA 2000007061	A	20010718	ZA 2000-7061	20001130
US 6387944	B1	20020514	US 2000-719047	20001207
US 2002045583	A1	20020418	US 2001-773772	20010202
US 6441022	B2	20020827		
PRIORITY APPLN. INFO.:			DE 1998-19825804	19980610
			AU 1997-23266	19970311
			WO 1999-EP3701	19990528
			US 1999-398315	19990920

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. such as I (mixture of diastereoisomers) were prepared as hypolipemic agents. Thus, I was prepared in 2 sequences from racemic II and Fmoc-D-lys(Boc)-OH, followed by removal of the Fmoc group with Et2NH. I was ≥20 times more active than 3 analogous comparison substances in tests of fecal separation of 14C-taurocholic acid in rats.

IC ICM C07D337-08
ICS C07K005-068; A61K031-38

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST amino acid benzothiepine dioxide deriv prepn hypolipemic

IT Hypolipemic agents
(amino acid containing benzo[b]thiepine 1,1-dioxide derivs. as)

IT 252372-02-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(amino acid containing benzo[b]thiepine 1,1-dioxide derivs. as hypolipemic agents)

IT 92122-45-7 252047-42-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(amino acid containing benzo[b]thiepine 1,1-dioxide derivs. as hypolipemic agents)

IT 252372-00-2P 252372-01-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid containing benzo[b]thiepine 1,1-dioxide derivs. as hypolipemic agents)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 10 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 132:22884 MARPAT
TITLE: Preparation of benzothiepine-1,1-dioxides as

hypolipemics

INVENTOR(S): Frick, Wendelin; Enhsen, Alfons; Glombik, Heiner; Heuer, Hubert

PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland G.m.b.H., Germany

SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964409	A2	19991216	WO 1999-EP3743	19990529
WO 9964409	A3	20000302		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19825804	A1	19991216	DE 1998-19825804	19980610
DE 19825804	C2	20000824		
TR 200003634	T2	20010621	TR 2000-20000363	19990528
ES 2182535	T3	20030301	ES 1999-927784	19990528
PT 1086092	T	20030331	PT 1999-927784	19990528
CA 2334773	AA	19991216	CA 1999-2334773	19990529
AU 9945031	A1	19991230	AU 1999-45031	19990529
AU 752633	B2	20020926		
EP 1086113	A2	20010328	EP 1999-927802	19990529
EP 1086113	B1	20040211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
TR 200003632	T2	20010420	TR 2000-20000363	19990529
JP 2002517490	T2	20020618	JP 2000-553418	19990529
JP 3374129	B2	20030204		
NZ 508681	A	20020628	NZ 1999-508681	19990529
RU 2220141	C2	20031227	RU 2001-101499	19990529
AT 259372	E	20040215	AT 1999-927802	19990529
US 6221897	B1	20010424	US 1999-398315	19990920
AU 761249	B2	20030529	AU 2000-53394	20000816
ZA 2000007060	A	20010718	ZA 2000-7060	20001130
ZA 2000007061	A	20010718	ZA 2000-7061	20001130
NO 2000006251	A	20010207	NO 2000-6251	20001208
US 2002045583	A1	20020418	US 2001-773772	20010202
US 6441022	B2	20020827		
US 2003017996	A1	20030123	US 2002-201050	20020724
US 6642269	B2	20031104		
US 2004087648	A1	20040506	US 2003-606771	20030627

PRIORITY APPLN. INFO.:

DE 1998-19825804	19980610
US 1996-13119P	19960311
AU 1997-23266	19970311
WO 1999-EP3743	19990529
US 1999-398315	19990920

US 2001-773772 20010202
US 2002-201050 20020724

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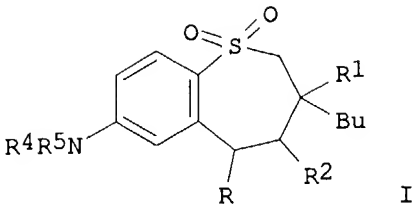

I

AB Title compds. [I; R = C6H4NHZR3; R1,R4,R5 = Me, Et, Pr, Bu; R2 = H, OH, amino(alkyl); R3 = sugar residue; Z = bond, carbonyl(alkylene), CONH, etc.] were prepared Thus, I [R = C6H4(NHR')-3, R1 = Et, R2 = OH, R4 = R5 = Me](II; R' = H) was amidated by penta-O-acetyl-D-gluconic acid and the product deprotected to give II (R' = gluconoyl) as a mixture of diastereomers. Data for biol. activity of I were given.

IC ICM C07D337-00

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST benzothiepine dioxide prepn hypolipemic

IT Hypolipemic agents
(benzothiepine-1,1-dioxides)

IT 252047-36-2P 252047-37-3P 252047-38-4P 252047-39-5P 252047-40-8P
252047-41-9P 252208-66-5P 252208-67-6P 252208-68-7P 252208-69-8P
252208-70-1P 252208-71-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzothiepine-1,1-dioxides as hypolipemics)

IT 488-43-7, D-Glucamine 2432-99-7, 11-Aminoundecanoic acid 17430-71-6, Penta-O-acetyl-D-gluconic acid 53555-69-4 252047-42-0 252047-43-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzothiepine-1,1-dioxides as hypolipemics)

IT 252047-44-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzothiepine-1,1-dioxides as hypolipemics)

L19 ANSWER 11 OF 13 MARPAT COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 131:58769 MARPAT

TITLE: Preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by cyclization of arylpropanalsulfoxides.

INVENTOR(S): Li, James; Wang, Ching-Cheng; Reitz, David B.; Snieckus, Victor; Huang, Horng-Chih; Carpenter, Andrew J.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932478	A1	19990701	WO 1998-US26216	19981216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9917213	A1	19990712	AU 1999-17213	19981216
EP 1042314	A1	20001011	EP 1998-962044	19981216
EP 1042314	B1	20030319		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001526284	T2	20011218	JP 2000-525415	19981216
BR 9814300	A	20020205	BR 1998-14300	19981216
AT 234829	E	20030415	AT 1998-962044	19981216
CN 1106395	B	20030423	CN 1998-813609	19981216
EP 1331225	A1	20030730	EP 2003-5459	19981216
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ES 2195428	T3	20031201	ES 1998-962044	19981216
ZA 9811648	A	19991220	ZA 1998-11648	19981218
AU 761249	B2	20030529	AU 2000-53394	20000816
US 6369220	B1	20020409	US 2000-581897	20001002
HK 1034971	A1	20040109	HK 2001-105743	20010815
US 2002188119	A1	20021212	US 2002-72600	20020211
CN 1439638	A	20030903	CN 2003-107046	20030228
PRIORITY APPLN. INFO.:			US 1997-68170P	19971219
			AU 1997-23266	19970311
			EP 1998-962044	19981216
			WO 1998-US26216	19981216
			US 2000-581897	20001002

OTHER SOURCE(S): CASREACT 131:58769
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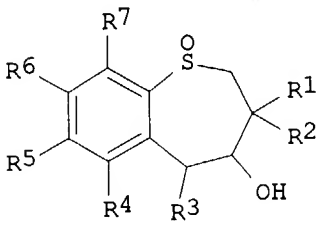

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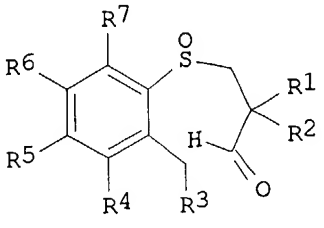

II

Searcher : Shears 571-272-2528

AB Title compds. [I; R1, R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl; R3 = H, (substituted) alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, etc.; R4-R7 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, halo, alkoxy, aryloxy, NO2, amino; R3 and the OH are syn], were prepared by cyclization of enantiomerically-enriched aldehydes (II; R1-R7 as above). Thus, enantiomerically-enriched II (R1, R2 = Bu; R4, R6, R7 = H; R5 = F; R3 = 4-MeOC6H4) (preparation given) was stirred with KOCMe3 in THF at -15° to give 77.7% (4R,5R)-I (variables as before).

IC ICM C07D337-08
ICS C07D487-08; C07D487-08; C07D241-00; C07D241-00

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))

ST benzothiepine oxide enantiomerically enriched prepn; arylpropanalsulfoxide enantiomerically enriched cyclization

IT Cyclization
(preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by
cyclization of arylpropanalsulfoxides)

IT 127184-05-8 139628-16-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(chiral oxidant; preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by cyclization of arylpropanalsulfoxides)

IT 135620-04-1
RL: CAT (Catalyst use); USES (Uses)
(chiral oxidation catalyst; preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by cyclization of arylpropanalsulfoxides)

IT 228113-61-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantiomerically-enriched; preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by cyclization of arylpropanalsulfoxides)

IT 546-68-9, Titanium tetraisopropoxide 13811-71-7, Diethyl D-tartrate
RL: CAT (Catalyst use); USES (Uses)
(preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by
cyclization of arylpropanalsulfoxides)

IT 228113-62-0P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by
cyclization of arylpropanalsulfoxides)

IT 75-91-2, tert-Butyl hydroperoxide 80-15-9, Cumyl hydroperoxide 93-59-4, Benzoyl hydroperoxide 124-40-3, reactions 371-41-5, 4-Fluorophenol 596-75-8, Diethyl dibutylmalonate 824-94-2, 4-Methoxybenzyl chloride 3071-34-9, Benzyl hydroperoxide 3240-34-4, Iodobenzene diacetate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by
cyclization of arylpropanalsulfoxides)

IT 1426-54-6P 3670-91-5P 24765-57-9P, 2,2-Dibutyl-1,3-propanediol 197378-20-4P 228113-57-3P 228113-58-4P 228113-59-5P 228113-60-8P

228113-65-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by
cyclization of arylpropanalsulfoxides)
IT 228113-63-1P 228113-64-2P 228113-66-4P 228113-67-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of enantiomerically-enriched tetrahydrobenzothiepine oxides by
cyclization of arylpropanalsulfoxides)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 12 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 129:260353 MARPAT
TITLE: Preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors.
INVENTOR(S): Reitz, David B.; Lee, Len F.; Li, Jinglin J.; Huang, Horng-Chih; Tremont, Samuel J.; Miller, Raymond E.; Baneriee, Shyamal C.; Manning, Robert E.; Glenn, Kevin C.; Keller, Bradley T.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; et al.
SOURCE: PCT Int. Appl., 477 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840375	A2	19980917	WO 1998-US3792	19980310
WO 9840375	A3	19981203		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9864408	A1	19980929	AU 1998-64408	19980310
AU 730024	B2	20010222		
EP 971744	A2	20000119	EP 1998-910075	19980310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 337830	A	20010727	NZ 1998-337830	19980310
BR 9808013	A	20010925	BR 1998-8013	19980310
JP 2002500628	T2	20020108	JP 1998-539594	19980310
NO 9904390	A	19991104	NO 1999-4390	19990910
AU 761249	B2	20030529	AU 2000-53394	20000816
US 2003171426	A1	20030911	US 2002-76091	20020215
US 6642268	B2	20031104		
PRIORITY APPLN. INFO.:			US 1997-40660P	19970311

US 1994-305526 19940913
US 1995-517051 19950821
US 1996-13119P 19960311
AU 1997-23266 19970311
US 1997-816065 19970311
US 1997-831284 19970331
WO 1998-US3792 19980310
US 2000-676466 20000929

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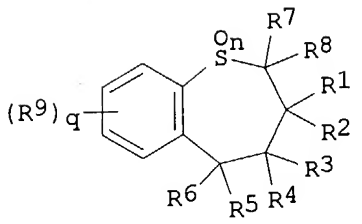

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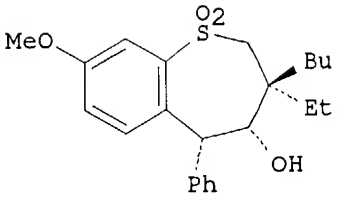

II

AB Title compds. [I; q = 1-4; n = 0-2; R1, R2 = H, (substituted) alkyl, alkenyl, alkynyl, haloalkyl, alkylaryl, alkoxy, dialkylamino, etc.; R1R2C = cycloalkylidene; R3, R4 = H, alkyl, alkenyl, alkynyl, acyloxy, aryl, heterocyclyl, heteroaryl, etc.; R3R4 = O, S, NOR11, etc.; R11 = H, alkyl, alkenyl, alkynyl, aryl, aralkyl, etc.; R5, R6 = H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, etc.; R7, R8 = H, alkyl; R9 = H, alkyl, alkenyl, alkynyl, acyloxy, aryl, aralkyl, halo, etc.], were prepared A composition comprising an ileal bile acid transport inhibitor and an HMG Co-A reductase inhibitor is claimed. Thus, title compound (II) (preparation via 2-mercapto-4-methoxybenzophenone given) at 0.2% as an ileal perfusion in guinea pigs reduced HDL cholesterol from 89 mg% to 76 mg%.

IC ICM C07D337-00

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST benzothiepine prepn bile acid transport inhibitor; antihyperlipidemic benzothiepine HMG reductase inhibitor

IT Hypolipemic agents
(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

IT Bile acids
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(transport inhibitors; preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

IT 178678-22-3P 178678-23-4P 178678-24-5P 178678-25-6P 178678-26-7P
178678-27-8P 178678-28-9P 178678-29-0P 178678-30-3P 178678-31-4P
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178678-54-1P 178897-95-5P 178897-96-6P 178897-97-7P 178897-98-8P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

IT 197375-57-8P 197375-60-3P 197375-63-6P 197375-66-9P 197375-68-1P
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Searcher : Shears 571-272-2528

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(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

IT 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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IT 100-35-6, 2-Diethylaminoethyl chloride 100-47-0, Benzonitrile, reactions 100-66-3, Anisole, reactions 108-98-5, Benzenethiol, reactions 110-86-1, Pyridine, reactions 110-91-8, Morpholine, reactions 123-75-1, Pyrrolidine, reactions 124-40-3, Dimethylamine, reactions 131-57-7, 2-Hydroxy-4-methoxybenzophenone 150-76-5 371-41-5, 4-Fluorophenol 503-29-7, Azetidine 696-63-9, 4-Methoxythiophenol 705-29-3, 3-Trifluoromethylbenzyl chloride 824-98-6, 3-Methoxybenzyl chloride 922-63-4, 2-Ethylacrolein 1481-12-5 1680-78-0, 2-Ethyl-2-hydroxymethylhexanal 1801-99-6, 2-Mercaptobenzophenone 2043-61-0, Cyclohexanecarboxaldehyde 2516-96-3, 2-Chloro-5-nitrobenzoic acid 2646-90-4, 2,5-Difluorobenzaldehyde 4521-31-7, 2-Mercaptobenzyl alcohol 5188-07-8, Sodium methanethiolate 13331-27-6,

3-Nitrobenzeneboronic acid 18982-54-2, 2-Bromobenzyl alcohol 24765-57-9, 2,2-Dibutyl-1,3-propanediol 25784-91-2, 2-Chloro-5-nitrobenzoyl chloride 28994-41-4, 2-Hydroxydiphenylmethane 34052-37-4, 2-Chloro-5-nitrobenzophenone 35730-09-7, 2,5-Difluorobenzoyl chloride 36839-55-1, 1,2-Bis(2-iodoethoxyethane) 128114-91-0 197372-97-7 197372-98-8 197375-48-7 197375-49-8 197378-48-6 197378-59-9 197378-60-2 213312-71-1 213312-75-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of ileal bile acid transport inhibiting benzothiepines for combination therapy with HMG Co-A reductase inhibitors)

L19 ANSWER 13 OF 13 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 127:307312 MARPAT
TITLE: Novel benzothiepines having activity as inhibitors of ileal bile acid transport and taurocholate uptake
INVENTOR(S): Reitz, David B.; Lee, Len F.; Li, Jinglin J.; Huang, Horng-Chih; Tremont, Samuel J.; Miller, Raymond E.; Banerjee, Shyamal C.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Reitz, David B.; Lee, Len F.; Li, Jinglin J.; Huang, Horng-Chih; Tremont, Samuel J.; Miller, Raymond E.; Banerjee, Shyamal C.
SOURCE: PCT Int. Appl., 406 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733882	A1	19970918	WO 1997-US4076	19970311

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RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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RU 2202549	C2	20030420	RU 1998-118643	19970311
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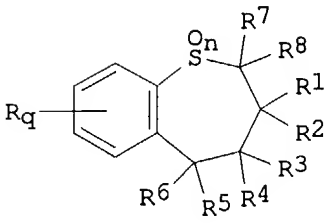

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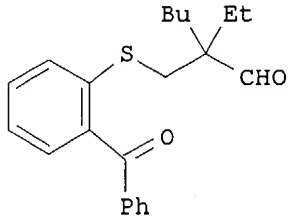

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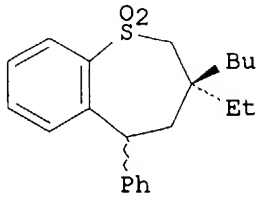

III

AB Novel benzothiepines I [q = 1-4; n = 0-2; R = H, halo, (un)substituted alk(en/yn)yl, acyloxy, aryl, heterocyclyl, OH or NH2 or SH or derivs., etc.; R1, R2 = H, (un)substituted and/or heteroatom-replaced alk(en/yn)yl, cycloalkyl, aryl, alkoxy, alkylthio, dialkylamino; or CR1R2 = C3-10

cycloalkylidene; R3, R4 = H, alk(en/yn)yl, acyloxy, aryl, heterocyclyl, OH or NH2 or SH or derivs.; or R3R4 = O, S, NH, NOH, NNH2, CH2 or derivs.; R5, R6 = H, (un)substituted alk(en/yn)yl, cycloalkyl, aryl, heterocyclyl, OH or SH or derivs.; R7, R8 = H, alkyl] and their derivs. and analogs are provided. Also provided are pharmaceutical compns. containing I and methods of their medical use, particularly in the prophylaxis and treatment of hyperlipidemic conditions, such as those associated with atherosclerosis or hypercholesterolemia. For instance, the keto aldehyde II was cyclized by Zn/TiCl3, and the resultant cycloolefin was oxidized and epoxidized by m-ClC6H4C(O)OOH and hydrogenated over Pd/C to give epimeric title compds. α- and β-III in 25% and 13% yield, plus addnl. compds. In a test for inhibition of IBAT-mediated uptake of [14C]-taurocholate in H14 cells in vitro, β-III had an IC50 of 5 μM.

IC ICM C07D337-08
ICS C07D409-10; C08G065-329; A61K031-38

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST benzothiepine prepn antihyperlipidemic antihypercholesterolemic antiatherosclerotic; bile acid transport inhibitor benzothiepine prepn; taurocholate uptake inhibitor benzothiepine prepn

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of benzothiepines as antihyperlipidemics)

IT Intestine
(ileum, inhibitors of ileal bile acid transport; preparation of benzothiepines as antihyperlipidemics)

IT Bile acids
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors of ileal bile acid transport; preparation of benzothiepines as antihyperlipidemics)

IT Anticholesteremic agents
Hypolipemic agents
(preparation of benzothiepines as antihyperlipidemics)

IT 197378-62-4P
RL: BYP (Byproduct); PREP (Preparation)
(byproduct; preparation of benzothiepines as antihyperlipidemics)

IT 81-24-3, Taurocholic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors of taurocholate uptake; preparation of benzothiepines as antihyperlipidemics)

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(intermediate; preparation of benzothiepines as antihyperlipidemics)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of benzothiepines as antihyperlipidemics)

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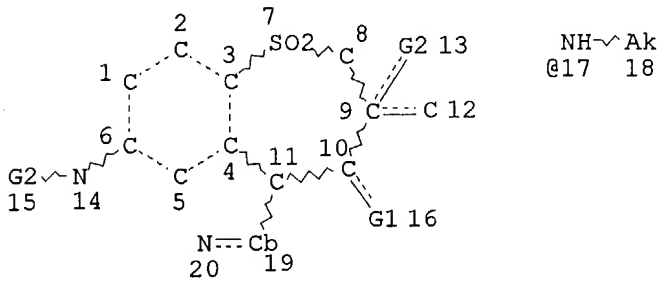
197384-36-4P 197384-39-7P 197390-49-1P 197390-68-4P 213386-72-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzothiepines as antihyperlipidemics)

IT 99-60-5, 2-Chloro-4-nitrobenzoic acid 100-47-0, Benzonitrile, reactions

100-66-3, reactions 106-41-2, 4-Bromophenol 110-91-8, Morpholine, reactions 123-75-1, Pyrrolidine, reactions 131-57-7, 2-Hydroxy-4-methoxybenzophenone 150-76-5, p-Methoxyphenol 352-11-4, 4-Fluorobenzyl chloride 371-41-5, 4-Fluorophenol 462-06-6, Fluorobenzene 503-29-7, Azetidine 629-09-4, 1,6-Diiodohexane 693-23-2, Dodecanedioic acid 696-63-9, 4-Methoxythiophenol 705-29-3, 3-(Trifluoromethyl)benzyl chloride 824-98-6, 3-Methoxybenzyl chloride 869-24-9, 2-(Diethylamino)ethyl chloride hydrochloride 922-63-4, 2-Ethylacrolein 1120-71-4, 1,3-Propanesultone 1680-78-0, 2-Ethyl-2-(hydroxymethyl)hexanal 1801-99-6, 2-Mercaptobenzophenone 2043-61-0, Cyclohexanecarboxaldehyde 2516-96-3, 2-Chloro-5-nitrobenzoic acid 2646-90-4, 2,5-Difluorobenzaldehyde 4509-90-4, 5-Bromovaleroyl chloride 4521-31-7, 2-Mercaptobenzyl alcohol 13331-27-6, 3-Nitrobenzeneboronic acid 15852-73-0, 3-Bromobenzyl alcohol 24765-57-9, 2,2-Dibutyl-1,3-propanediol 28994-41-4, 2-Hydroxydiphenylmethane 33663-73-9, 2-Chloro-4-nitrobenzophenone 34052-37-4, 2-Chloro-5-nitrobenzophenone 35730-09-7, 2,5-Difluorobenzoyl chloride 36839-55-1, 1,2-Bis(2-iodoethoxy)ethane 99376-14-4 121559-53-3 197378-59-9 197378-60-2 197378-61-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of benzothiepines as antihyperlipidemics)

FILE 'MARPATPREV' ENTERED AT 09:34:05 ON 26 AUG 2004

L16 STR



VAR G1=H/OH/NH/17
VAR G2=ME/ET/I-PR/N-PR/I-BU/N-BU/S-BU/T-BU
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 18 19
GGCAT IS LOC AT 18
GGCAT IS UNS AT 19
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L20 0 SEA FILE=MARPATPREV SSS FUL L16 (MODIFIED ATTRIBUTES)

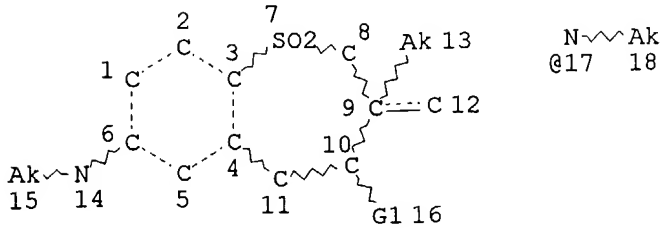
100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FILE 'HOME' ENTERED AT 09:34:22 ON 26 AUG 2004

Searcher : Shears 571-272-2528

(FILE 'REGISTRY' ENTERED AT 13:29:20 ON 26 AUG 2004)

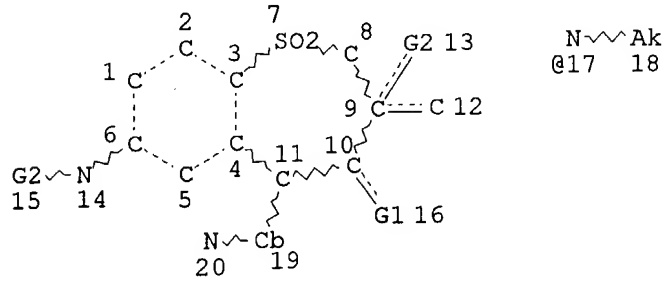
L1 STR



VAR G1=H/OH/NH/17
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L2 649 SEA FILE=REGISTRY SSS FUL L1
L4 STR



VAR G1=H/OH/NH/17
VAR G2=ME/ME/I-PR/N-PR/I-BU/N-BU/S-BU/T-BU
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 18
GGCAT IS UNS AT 19
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L5 107 SEA FILE=REGISTRY SUB=L2 SSS FUL L4
L6 72 SEA FILE=REGISTRY ABB=ON PLU=ON L5 AND 1/NC

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 13:32:11 ON 26 AUG 2004)
L7 0 S L6

FILE 'HOME' ENTERED AT 13:32:42 ON 26 AUG 2004

Searcher : Shears 571-272-2528